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THE INDICATIONS AND CONTRAINDICATIONS FOR CHOLECYSTECTOMY*

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THE INDICATIONS for immediate cholecystectomy are the presence of stones, their relation to the patient's complaints, and the existence of local complications. The degree of relief that a patient may receive from a cholecystectomy is conditioned by the type of individual afflicted and is in direct proportion to the relationship of all his complaints to the offending gallstones. Thus, if his symptoms are entirely due to the gallbladder disease, his recovery should be complete provided delay has not allowed the process to involve irreparably such structures as the common duct, pancreas or liver.

Unfortunately, the ideal circumstances which should lead to a perfect result are not always present in many cases requiring operation. A patient may justifiably require cholecystectomy for stones but if, in addition, he is suffering from flatulent dyspepsia of nervous origin, a spastic and irritable colon, peptic ulceration or coronary disease, the relief he obtains will be incomplete. Cholecystectomy, therefore, should be advised only after all the symptoms contributing to the patient's illness have been properly assessed. Most of these other factors have their origin outside the biliary tract. In this paper I shall attempt to place a clinical value upon some of them and to indicate how they should influence our decision for or against immediate surgical intervention.

This complex clinical problem resolves itself under three headings: (a) biliary calculi that are silent; (b) biliary calculi with dyspepsia only; (c) biliary calculi with dyspepsia and pain.

(a) *Silent calculi.*—Concerning the first, the simplest conclusion would be to advise the removal of all gallstones "on discovery" because of the possible danger of future complications. These include perforation with peritonitis or abscess, common duct stone, jaundice, suppurative cholangitis, hepatitis, pancreatitis, carcinoma of the gallbladder, duodenal fistula, and small bowel obstruction due to impaction of a gallstone in the terminal ileum. This is surely a formidable array of complications that might be prevented by routine cholecystectomy for stones. Under ideal conditions it is now possible to perform a large series of cholecystectomies in uncomplicated cases without a death and with very little morbidity.

The foregoing reasons are all impressive and true to an important degree but yet do not justify routine cholecystectomy "on discovery" in all cases of gallstone disease. There are other important aspects to this clinical problem. Our attitude towards routine surgical intervention must be tempered by the fact that there is a high incidence of silent gallstones that never cause trouble. Furthermore, patients are not always relieved of their dyspepsia and pain by cholecystectomy.

Fifteen to 18 per cent of gallstones contain sufficient calcium to appear on any x-ray film of the abdomen or lower chest taken for other reasons than the clinical suspicion of disease in the biliary apparatus. Again, gallstones may be discovered during laparotomy for other intra-abdominal or pelvic disease.

Under these circumstances the patient should be acquainted with their presence. To withhold this information in order to protect him from anxiety is, from my experience with a great many nervous and apprehensive patients, quite unjustified. Almost without exception, patients will accept the physician's frank explanation of the situation. If the patient is unstable, going from one physician to another, he will soon learn of the "deception," which he ascribes to a mistake in diagnosis. A result of this will be an in-

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crease in his lack of confidence in the medical profession and aggravation of his anxieties.

In an otherwise normal individual without symptoms and in whom the gallbladder is diseased and full of stones, operation can be performed without fear of troublesome sequelæ of a functional nature. It is in the hypochondriac that one may find the resultant condition of the patient worse than his preoperative state. Obviously, we cannot formulate a policy which will cover all cases in which stones are silent or all patients whose complaints are such that one has good reason to suspect a mainly functional origin for many of them.

The patient who has a normally functioning gallbladder with a round, single, transparent stone situated in the centre of the opaque medium, and in whom one has good reason to suspect a highly functional element, should not be advised to have an immediate cholecystectomy. Such a stone is usually a smooth, pure cholesterol calculus and represents the end result of a metabolic disturbance in the biliary system which, fortunately for the patient, has not resulted and may not result in serious interference with the function of the gallbladder. In my experience at least, it does not justify surgical interference when first recognized unless it is obviously a troublemaker.

(b) *Biliary calculi with dyspepsia only.*—We must use particular discretion in advising cholecystectomy for stones in patients whose flatulent dyspepsia is associated with chronic or recurrent nervous exhaustion. If there is a reasonable doubt that the epigastric distress is related to the presence of calculi, a trial period of dietary and medicinal therapy is advisable. Such an attitude permits the patient to understand that some of his complaints may not be due to the gallstones alone and that his gastric distress may be controlled or modified by proper dietary habits. During this period also, he should be informed concerning the part emotional or nervous factors play in recurrent gastrointestinal upsets. He will thereby be protected against the disappointment which may follow precipitate surgery before due consideration is given to these other factors. Following a period of comprehensive medical management the need for operation can be discussed with the patient.

There are experienced clinicians who advise routine immediate operation for gallstones "on discovery" because of their experience of serious and sometimes fatal complications. On the other hand, there are clinicians who refuse to advise surgery unless complications are threatened, imminent or already present. It is surprising to me how many excellent clinicians hold these extreme views. From the point of view of the patient afflicted with gallstones and also in order to clarify our teaching to senior medical students and interns, the advocates of these extreme views might well re-examine their position in the light of the experience of those in the opposite camp.

(c) The subject of *biliary calculi with pain or colic* should need no special emphasis if it were not for the fact that a major portion of our surgical difficulties in connection with gallbladder disease is due to unwarranted delay in advising operation after the first attack of biliary colic and its recognition. Recurrent attacks of cystic duct obstruction by stone produce dense pericholecystic adhesions with distortion of the normal anatomical relationships. Extension of the disease to involve the common duct, the liver and the pancreas results in protracted and at times incomplete recovery after operation. The local technical difficulties in performing a safe cholecystectomy are due to these later complications which, in many instances, could be avoided by earlier operation. The medical man who fails to advise operation earlier in the presence of established gallbladder disease must share equally with the surgeon the responsibility for some of the unsatisfactory results following cholecystectomy. There are five main causes for failure in gallstone surgery:

1. Incomplete history and preoperative investigation (resulting in a partial diagnosis only).
2. Poor selection and preparation of patients for surgery in the group in which flatulent dyspepsia and nervous instability are present.
3. The removal of a non-calculous gallbladder, because of failure to perform cholecystography at least twice for a non-functioning gallbladder.
4. Technical errors such as failure to remove stones from the common duct or incomplete removal of the cystic duct containing small calculi.
5. Delay in surgical treatment until common duct infection and stones and hepatic or pancreatic involvement have occurred.

The indications for and the contraindications to cholecystectomy may be summarized as follows:

1. The mere presence of calculi is not always adequate justification for immediate cholecystectomy. Other factors contributing to the patient's symptoms may have priority in treatment.

2. Age or infirmity due to other serious organic disease has to be considered in determining the need, the time and the extent of the operation.

3. A known typhoid carrier should be advised to have cholecystectomy because chloramphenicol is ineffective in eradicating infection in the chronic carrier state.

4. Gallbladder disease with stones is of importance in diabetic patients because the gallbladder may act as an intermittent focus of infection, making the diabetes more difficult to control. The relationship of cholelithiasis to pancreatitis must also be borne in mind in diabetic patients, as bouts of pancreatitis tend to cause further pancreatic damage and may increase the severity of the diabetes and complicate its management. Diabetes is, therefore, at times an added indication for cholecystectomy in the presence of stones.

5. Gallbladder and coronary artery disease are frequently associated and the symptoms of one may simulate the symptoms of the other. It is, therefore, of great importance to differentiate between the two conditions. It is well known that acute cholecystitis or gallstone colic and pancreatitis, as well as other acute abdominal lesions, may affect the electrocardiogram either in the presence or absence of cardiac symptoms. It has been demonstrated that gallbladder disease may act as a trigger to reveal coronary artery disease. Experimentally, it has been shown that distension and irritation of the gallbladder or its ducts initiate afferent impulses in the vagus nerve. These in turn produce efferent impulses of central reflex origin which may lead to coronary vasoconstriction. A person suffering from both symptomatic gallbladder disease and coronary artery disease will often have an amelioration of his symptoms of angina following cholecystectomy. Obviously, the underlying disease of the coronary arteries is not affected by such a surgical procedure.

6. A patient with gallstones who has flatulent dyspepsia only or an intolerance to fatty foods should not be advised to have immediate surgery for the purpose of relieving the dyspepsia. If the distress is extreme, surgery will be indicated ultimately but these patients should first be given a course of medical management. From the patient's point of view, it is preferable to operate after he has been subjected to some dietary discipline. In other words, he is informed that his trouble is only partly surgical and not urgent and that the medical aspect of his complaints cannot be ignored either before or after the operation.

7. A patient with a history of biliary colic, which need not be severe, and in whom a diagnosis of gallstones is established, should be advised to undergo a cholecystectomy without delay. While one should postpone operation in patients who have dyspepsia only, one should advocate a more positive attitude towards the patient who already has suffered one or more attacks of biliary colic. In this group of cases there is no justification for postponing an operation until serious local complications have developed as the result of repeated attacks of colic and œdema of the gallbladder wall. Also in the more insidious form in which dyspepsia and chronic recurrent epigastric pain can be ascribed to chronic gallbladder disease with stones, early operation should be advised. The relatively normal gallbladder containing many small stones which can cause intermittent obstruction of the cystic duct is often a greater menace to the patient than a large thickened gallbladder completely packed with stones.

While it is true that I have spent long hours for many years in an attempt to correct the end results of misdirected conservatism in the treatment of calculous disease of the gallbladder, I cannot subscribe to the view that the presence of gallstones alone is sufficient justification for immediate cholecystectomy in all cases. Such an attitude is comparable to removing every uterus for all fibroids, every breast for cystic disease, every thyroid because of enlargement or irregularity in its contour.

In order that we may reduce the incidence of persistent postoperative complaints, may I recapitulate certain basic considerations applicable to this problem.

1. Complete preoperative investigation and full clinical assessment of the individual case. This may require the combined judgment and experience of the internist and the surgeon.

2. Comprehensive medical management, including psychological and dietary adjustment, especially in cases where emotional instability and recurrent nervous exhaustion complicate the clinical picture.

3. Earlier operation when gallbladder disease with stones is proved and the history reveals minor or severe attacks of cystic duct obstruction or recurrent epigastric distress and dyspepsia.

4. Gallstone disease and its complications is primarily a surgical problem. In many patients, however, cholecystectomy with or without common duct exploration is but one important step in the total management of this common disorder.

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RÉSUMÉ

Les indications en faveur de la cholécystectomie immédiate sont la présence de calculs, leur part dans les douleurs du malade, et les complications locales. Si un malade présente des symptômes d'une affection de la vésicule biliare seulement, la guérison devrait résulter de l'opération exécutée à temps. Par contre, chez un malade souffrant en plus de flatulence et de dyspepsie d'origine nerveuse, par exemple, la guérison ne saurait être complète. On peut classer les calculs biliaires comme suit: (A) les calculs biliaires asymptômatiques; (B) les calculs biliaires accompagnés de dyspepsie seulement; (C) les calculs biliaires accompagnés de dyspepsie et de coliques.

(A) Ce serait une erreur de croire qu'il vaudrait mieux enlever tous calculs biliaires asymptômatiques dès qu'on les découvre, simplement à cause des dangereuses complications auxquelles ils peuvent donner lieu. Un grand nombre de formes frustes restent toujours inoffensives. On doit informer le malade chez qui on découvre accidentellement des calculs biliaires. Un individu normal dont la vésicule est remplie de calculs silencieux subira généralement l'opération avec succès. Un hypochondriaque pourra, au contraire, se sentir plus mal après qu'avant l'intervention. On doit déconseiller la cholécystectomie immédiate chez un malade dont la vésicule fonctionne normalement tout en renfermant un seul calcul rond et transparent, probablement de cholestérol pur, dû à un dérangement fonctionnel du système biliaire.

(B) La cholécystectomie doit être considérée avec grande prudence dans le cas des malades souffrant de flatulence et de dyspepsie en relation avec un épuisement nerveux chronique ou périodique. Il faut essayer les traitements médicaux et les régimes alimentaires appropriés et avertir le malade de l'influence sur son état des facteurs émotifs et nerveux. On évitera ainsi son désappointement s'il subit une opération qui n'apporte pas la guérison complète.

(C) Dans les cas de calculs biliaires avec coliques, on recommande l'opération après la première crise de douleur, sous peine de graves difficultés dans la guérison si l'opération est indûment retardée. Il y a cinq causes principales à l'échec de la cholécystectomie:

1. l'interrogatoire et l'examen sont incomplets, résultant en un diagnostic mal fondé;
2. le fait d'opérer sans distinction ni préparation les malades souffrant en plus de dyspepsie et d'instabilité nerveuse;
3. l'ablation d'une vésicule sans calcul, parce qu'on n'a pas réussi la cholécystographie d'une vésicule ne fonctionnant pas;
4. des erreurs techniques, comme de laisser des calculs dans le canal hépatique, ou l'ablation incomplète d'un canal cystique contenant de petits calculs;
5. retard à l'opération et développement de complications.

La cholécystectomie est recommandée dans les cas de calculs chez les porteurs de germes de typhoïde, et quelquefois chez les diabétiques. On doit prendre garde de ne pas confondre la cholécystite aiguë, la colique hépatique et la pancréatite avec les manifestations de l'insuffisance coronarienne. M.R.D.

STAINABLE FERRIC IRON PARTICLES IN ERYTHROID MARROW CELLS AND ERYTHROCYTES*

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SMALL PARTICLES of non-hæmoglobin iron, stainable with potassium ferrocyanide and hydrochloric acid, were first demonstrated in human erythrocytes a decade ago.[1] These inclusions have been conspicuous in peripheral blood cells of some patients after splenectomy, notably in acquired hæmolytic anæmia.[2, 3] Pappenheimer[2] observed large numbers after this operation in a case of chronic hypochromic anæmia of unknown etiology associated with splenomegaly. Anæmia associated with similar findings has been familial in a few instances.[4, 5, 6] The stippled erythrocytes in lead poisoning often contain stainable iron particles.[7]

Erythrocytes containing siderotic granules stainable with potassium ferrocyanide and hydrochloric acid have been called *siderocytes* by Grüneberg[8] and his definition will be applied to the term in this paper. The siderotic granules demonstrated in erythrocytes by Case[9] require a different stain[3] and should not be confused with those under discussion.

Attention was called to inclusions in the fully

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hæmoglobinated normoblasts of the marrow by McFadzean and Davis.[3] These bodies are located in the cytoplasm of the cells and show morphology and staining properties similar to those within siderocytes. Normoblasts containing such bodies have been called *sideroblasts.*[10] The observations that the inclusions occurred in a greater proportion of normoblasts than of erythrocytes, and that their relative frequency in the former cell type was unaffected by splenectomy, suggested that the bodies were formed during erythropoiesis, and that more reliable information concerning the proportion of erythrocytes affected at the time of their formation would be obtained by a study of the nucleated rather than non-nucleated red cells.[3, 7] It was suggested that the intact spleen removed siderocytes from the blood selectively. This statement was supported by evidence that splenectomy improved the anæmia of lead poisoning, and the idiopathic hæmolytic anæmia with a high sideroblast count, in proportion to the increment of circulating siderocytes after this operation. No correlation was observed between the frequency of siderocytes and that of reticulocytes in the blood.

A more recent study[10] has suggested that sideroblasts are present in marrow aspirates from normal persons in larger numbers than were previously reported, and that iron deficiency is indicated where less than 15% of hæmoglobinated normoblasts show stainable iron granules. High counts were obtained in thalassæmia and lead poisoning. The wide discrepancy between these findings and the very low counts previously reported on normal marrow aspirates[3] suggested that slight differences in technique or interpretation altered the proportion of reported sideroblasts very appreciably. Both groups of investigators found high sideroblast counts in lead poisoning, rendering it likely that they were counting the same type of cell. Possibly in other conditions the granules were smaller or more faintly stained and consequently the affected cells were classified differently in the two reports. Differences in the hæmoglobin content required to render a normoblast countable could also explain part of the discrepancy.

During the course of a study of the stainable iron concentration in the reticulo-endothelial cells of aspirated bone marrow particles in disease,[11] large numbers of sideroblasts were observed as an incidental finding in a case of thalassæmia and two cases of idiopathic erythræmic myelosis.* The findings were considered to be of sufficient interest to make a search for these cells in marrow aspirates from a variety of diseases concurrent with clinical appraisal, estimation of body storage iron and serum iron determinations.

MATERIAL AND METHODS

Marrow aspirates were studied from 68 persons. Nine persons showed no evidence of anæmia or excessive iron stores, and hypoferræmia was excluded or considered to be unlikely. Eleven persons had iron deficiency anæmia, and 19 had anæmia associated with inflammatory disease. Twenty-six persons had various other types of anæmia, three were not anæmic but had conditions often associated with hypoferræmia, and one had hæmochromatosis.

Small fragments of marrow tissue were selected from the sternal aspirates and spread gently between coverslips. The unfixed fragments were stained for 30 minutes using the method of Rath and Finch.[12] The Berlin blue stain was prepared by adding concentrated hydrochloric acid to a 20% solution of potassium ferrocyanide. When the white precipitate persisted after stirring, the solution was filtered and used immediately. A faint counterstain was applied to the cells, using a dilute aqueous solution of basic fuchsin followed by 95% alcohol differentiation. The cell suspension deposited around the marrow tissue fragments was examined with oil immersion magnification (ocular x 10) of a Bausch and Lomb binocular microscope. The late normoblasts were readily detected by the presence of unstained hæmoglobin in their cytoplasm. One hundred cells containing a large complement of this pigment were counted, and the number containing blue cytoplasmic granules was recorded. The same procedure was used in counting *siderocytes* in peripheral blood, except that 100 erythrocytes instead of normoblasts were classified by the presence or absence of stainable iron granules.

A small number of preparations were rejected after staining because hæmoglobin was no longer detectable in the erythrocytes and normoblasts. The sideroblast counts were not altered by fixing the aspirated marrow with

*For definition, see "Discussion."

Canad. M. A. J.
Mar. 15, 1955, vol. 72

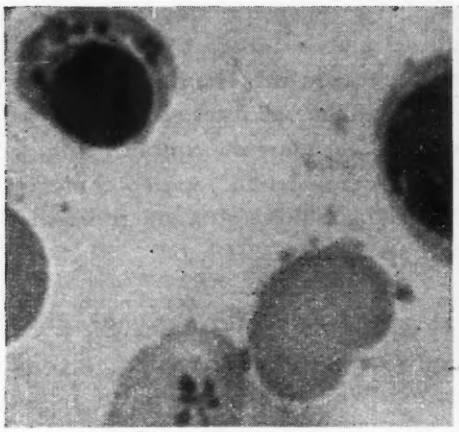

Fig. 1

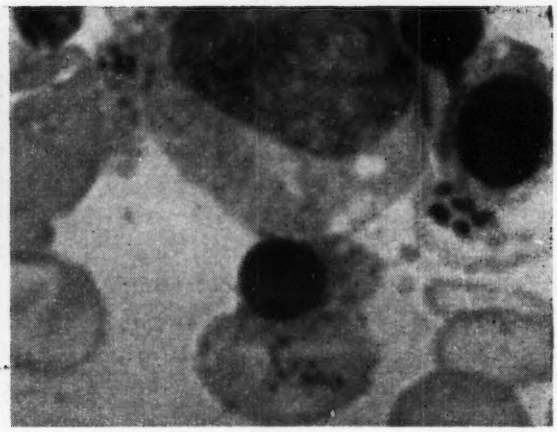

Fig. 2

Fig. 1.—Sideroblast and siderocyte from bone marrow in thalassæmia. The dark cytoplasmic inclusion bodies permit identification of these cells. Wright's stain x 2000. **Fig. 2.**—Siderocytes from bone marrow in thalassæmia. Note the grouping of the inclusion bodies and the presence of hypochromia. Wright's stain x 2000.

formalin vapour, absolute methanol or ethanol. A staining solution consisting of equal parts of 4% potassium ferrocyanide (allowed to age for eight days) and 4% hydrochloric acid was compared with that described above; the sideroblast counts were essentially the same.

The stainable iron content of the reticuloendothelial cells in the marrow fragments was used as a rough indication of the body iron stores and was graded arbitrarily from 0.0 to 6.0. The method of grading is described elsewhere.[11] The average value in normal persons varied from grade 2.1 to 3.0, with a wide range around these figures.

Oxyhæmoglobin concentration was measured in the Coleman Junior spectrophotometer[13] standardized against the oxygen capacity of venous blood. The serum iron concentration was measured by the method of Kitzes, Elvehjem and Schuette,[14] normal values in this laboratory ranging from 62 to 182 μg. %. The unsaturated iron binding capacity of the serum was determined by the method of Cartwright and Wintrobe.[15] The total iron binding capacity (normal values ranging from 242 to 382 μg. %) was obtained by adding the serum iron level to the unsaturated iron binding capacity. Further detail concerning the use of these methods is reported elsewhere.[11]

RESULTS

The colour of siderotic granules visible in Wright's stained preparations was indistinguishable from that of Howell-Jolly bodies. However, two or more of the former were sometimes grouped in a characteristic manner at the periphery of an erythrocyte (Figs. 1 and 2), and occasionally an affected cell showed more hypo-

TABLE I.

SIDEROBLAST COUNTS AND OTHER DATA IN NINE CASES WITHOUT EVIDENCE OF ANÆMIA OR EXCESSIVE IRON STORES AND WHERE HYPOFERRÆMIA HAS BEEN EXCLUDED OR IS UNLIKELY

Name	*Diagnosis*	*Marrow aspirate B.B.P.* grading (graded 0 to 6)*	*Serum iron (μg. %)*	*Marrow sideroblasts (% of late normoblasts)*
R.St.	Congestive heart failure	3.0		3
N.McI.	Pulmonary tuberculosis, repeated hæmoptysis	0.0	82	3
G.S.	Tabes dorsalis, bleeding hæmorrhoids	0.0	95	5
A.M.	Carcinoma of stomach, total gastrectomy	2.3	98	14
V.N.	Chronic neutropenia	0.0		22
Q.F.	No apparent disease	2.5		24
J.Cr.	Chronic neutropenia	2.0		40
C.Wa.	Bronchogenic carcinoma, pulmonary tuberculosis	2.0	92	42
H.McI.	Rheumatic heart disease, secondary erythrocytosis	2.1		43
Mean		1.5	91	22

*B.B.P. = Berlin blue positive.

TABLE II.

SIDEROBLAST COUNTS AND OTHER DATA IN 11 CASES OF IRON DEFICIENCY ANÆMIA

Name	*Diagnosis*	*Hæmoglobin concentration (gm. %)*	*Marrow aspirate B.B.P. grading (graded 0 to 6)*	*Serum iron (μg. %)*	*Marrow sideroblasts (% of late normoblasts)*
P.G.	Gastro-intestinal hæmorrhage	4.4	0.0	27	0
T.G.	Idiopathic hypochromic anæmia	8.1	0.0	12	0
A.S.	Idiopathic hypochromic anæmia	8.3	0.0	33	2
E.H.	Rheumatic heart disease	8.6	0.0		2
K.S.	Hyperthyroidism, rheumatic heart disease	7.8	0.0		3
D.C.	Carcinoma of colon	9.2	0.0		3
B.McG.	Thrombocytopathic purpura, primary amyloidosis	9.8	0.0		6
G.Co.	Renal tuberculosis	11.1	0.0	21	2
J.F.	Congestive splenomegaly, œsophageal varices	12.8	0.0		14
P.S.	Rheumatoid spondylitis	9.5	0.2	5	1
G.Cl.	Post-gastrectomy and splenectomy Treated megaloblastic anæmia	8.6	1.1	40	2
Mean			0.1	23	3

chromia than its fellows. Sideroblast and siderocyte counts were invariably higher when the iron stain was used than when attempts were made to identify the granules in Wright's stained preparations, so the latter were not used for enumeration.

Table I shows the sideroblast counts from nine persons without evidence of anæmia or excessive iron stores, in whom hypoferræmia was excluded or was unlikely. The mean value was 22%, with a range from 3 to 43%. Berlin blue positive (B.B.P.) material was not detectable in the reticulo-endothelial cells of the marrow fragments of three cases (N.McI., G.S., and V.N.), suggesting depleted iron stores. The depletion of total body iron was insufficient, however, to cause anæmia or hypoferræmia.

Table II shows the sideroblast counts from eleven patients with iron deficiency anæmia. The mean value was 3%, with a range from zero to 14%. It may be noted that the highest count occurred in the individual with the least degree of anæmia. The marrow aspirate B.B.P. grading of case G.Cl. was 1.1 although he was regarded as being iron deficient. There was evidence (Table IV) that his iron stores had not been

TABLE III.

SIDEROBLAST COUNTS AND OTHER DATA IN 19 CASES OF ANÆMIA AND INFLAMMATION

Name	*Diagnosis*	*Marrow aspirate B.B.P. grading (graded 0 to 6)*	*Serum iron (μg. %)*	*Marrow sideroblasts (% of late normoblasts)*
J.He.	Pulmonary tuberculosis	4.3	8	3
E.S.	Suppurative pulmonary disease	0.0	8	0
E.Cr.	Rheumatoid arthritis	1.3	9	6
J.C.	Pulmonary tuberculosis	0.3	16	5
J.M.	Rheumatoid arthritis	0.0	24	0
R.S.	Mixed arthritis	1.6	24	23
D.S.	Pulmonary tuberculosis	2.5	28	12
E.Ca.	Rheumatoid arthritis	0.0	28	2
J.L.	Pulmonary tuberculosis, neurosyphilis; urinary infection	3.5	30	0
E.G.	Pulmonary tuberculosis	5.2*	36	7
S.M.(2)	Rheumatoid arthritis	3.9†	39	7
F.G.	Rheumatoid spondylitis; pulmonary tuberculosis	0.9	39	14
S.M.(1)	Rheumatoid arthritis	2.5	40	0
B.H.	Rheumatoid arthritis	2.5	40	2
C.Wi.	Rheumatoid arthritis	0.7	43	2
M.M.	Rheumatoid arthritis	1.7	48	3
L.W.	Rheumatoid arthritis	4.0‡	50	26
F.O.	Chronic osteomyelitis	5.0*	85	44
E.P.	Rheumatoid spondylitis	0.0	92	72
J.E.	Urinary tract infection	3.3	110	40

*Following multiple blood transfusions.
†Following 1,400 mgm. intravenous saccharated iron oxide.
‡Following 1,950 mgm. intravenous saccharated iron oxide.

TABLE IV.

SIDEROBLAST COUNTS AND OTHER DATA IN THREE CASES OF THALASSÆMIA, TWO CASES OF ERYTHRÆMIC MYELOSIS AND SEVEN CASES OF MEGALOBLASTIC ANÆMIA

Name	*Diagnosis*	*Marrow aspirate B.B.P. grading (graded 0 to 6)*	*Serum iron (μg. %)*	*TIBC (μg. %)*	*Marrow sideroblasts (% of late nucleated red cells)*
S.D.	Thalassæmia	5.5*	165	212	95
G.L.	Thalassæmia	3.0†			74
B.M.	Thalassæmia	5.5†			83
F.B.	Idiopathic erythræmic myelosis	4.5			82
N.McM.	Idiopathic erythræmic myelosis	6.0‡	150	150	83
A.McD.	Pernicious anæmia	4.5			
G.W.	Pernicious anæmia	4.0			76
G.W.	17 days after starting vitamin B_{12}	3.0			9
C.N.	Pernicious anæmia	3.5			51
F.McC.	Pernicious anæmia of pregnancy	3.0			67
Hup.	Megaloblastic anæmia, partial gastrectomy and splenectomy	4.0	160	252	85
G.Cl.	Megaloblastic anæmia, total gastrectomy and splenectomy	2.9	42	132	81
G.Cl.	29 days after starting vitamin B_{12}	1.1	40	374	2
D.F.	Achrestic anæmia	3.0			56

*Following 850 mgm. intravenous saccharated iron oxide.
†No information on parenteral iron administration.
‡Following 5,500 c.c. transfused blood.

completely depleted when parenteral vitamin B_{12} therapy was initiated for the megaloblastic anæmia 29 days before the figures tabulated above were obtained. The rapid withdrawal of the remaining stores for erythropoiesis was followed by overt iron deficiency anæmia before sufficient time elapsed for iron to be removed from numerous small hæmosiderin granules in the marrow reticulo-endothelial cells. Consequently the B.B.P. grading was misleading.

Table III shows the sideroblast counts from 19 patients with anæmia and inflammatory disease. Case S.M. was studied on two occasions. The sideroblast counts were higher in the four patients with serum iron levels above 49 μg. % than in the others. Concurrent study of the effect of intravenous saccharated iron oxide in many of the patients showing hypoferræmia indicated that the anæmia was lessened by this therapy.[11] However, this agent was of no value in three patients with serum iron levels above 49 μg. % and sideroblast levels above 23%. The data suggested that the hypoferræmia of inflammation rendered the erythroid tissue relatively iron deficient, even though the iron stores were adequate. The mean sideroblast count of 15 patients with serum iron levels below 49 μg. % was 5% (Table III).

Table IV shows the sideroblast counts of three conditions in which high counts were regularly obtained. The range in three patients with thalassæmia was from 74 to 95%. In idiopathic erythræmic myelosis the tabulated values of two cases were 82 and 83%, but one patient (F.B.) showed up to 94% sideroblasts several months after receiving 4,500 ml. transfused blood (2.2 gm. iron). The serum iron level at this time was 197 μg. % with saturation of the iron binding protein. The marrow aspirate B.B.P. grading was 6.0. In pernicious anæmia and related forms of megaloblastic anæmia, the counts of six patients varied from 51 to 85%. Much lower values were obtained on two of these cases (G.W. and G.Cl.) after initiating parenteral vitamin B_{12} therapy.

Table V shows sideroblast counts from 18 other patients, 14 of whom were anæmic. Patients with conditions in which hypoferræmia was expected,[16] and one in whom this was demonstrated to be present, were grouped because the data in Tables II and III suggested that the sideroblast counts were influenced by low serum iron levels. The sideroblast counts from these were low with the exception of one individual (J.Ch.).

No consistent trend was observed in the sideroblast counts from four patients with severe hæmolytic anæmia. A positive Coombs test was obtained from the case (A.W.) showing a count of 68%. The sideroblast enumerations from six patients with impaired marrow function of unknown cause showed an equally wide range of values. A count of 63% was obtained from E.Cl., who showed the clinical features of "aplastic anæmia." The marrow was not abnormally hypo-

TABLE V.

SIDEROBLAST COUNTS AND OTHER DATA IN 18 CASES OF MISCELLANEOUS CONDITIONS

Name	*Diagnosis*	*Marrow aspirate B.B.P. grading (graded 0 to 6)*	*Serum iron (μg. %)*	*Marrow sideroblasts (% of late normoblasts)*
	Conditions often associated with hypoferræmia			
J.DeW.	Multiple myeloma with mild anæmia	0.0	25	1
M.B.	Reticulum cell sarcoma with mild anæmia	2.0		3
E.B.	Hodgkin's disease with no anæmia	2.2		2
F.E.	Polycythæmia rubra vera with bleeding duodenal ulcer	0.0		10
J.Ch.	Sarcoidosis with no anæmia	2.0		24
	Hæmolytic anæmias			
S.R.	Congenital hæmolytic jaundice	3.5		4
A.McI.	Erythroblastosis fœtalis	1.2		36
R.D.	Acquired hæmolytic anæmia; blood loss; portal cirrhosis; post-splenectomy	2.0*		5
A.W.	Acquired hæmolytic anæmia of unknown cause	2.5		68
	Impaired marrow function of unknown cause			
L.M.	Mild anæmia	4.7	50	38
M.B.	Mild anæmia	3.8†	67	42
E.Cl.	Functionally "aplastic" anæmia (idiopathic)	3.7‡	160	63
J.G.	Functionally "aplastic" anæmia (idiopathic)	5.0¶		27
A.M.	Functionally "aplastic" anæmia (idiopathic)	3.0		25
A.M.	Clinically unchanged 4 months later	4.7**	209	2
	Miscellaneous conditions			
J.De.	Anæmia and neutropenia following chloramphenicol	3.0		63
R.A.	Scurvy with anæmia after 5 days ascorbic acid	2.1	50	8
R. McG.	Congestive splenomegaly with mild anæmia	4.5		4
Bu.	Idiopathic hæmochromatosis	5.7	262	23

*Following 8,200 c.c. transfused blood.
†Following course of saccharated iron oxide.
‡Following 6,000 c.c. transfused blood.
¶Following 3,500 c.c. transfused blood.
**Following 7,000 c.c. transfused blood.

plastic, but showed a striking maturation arrest. Similar clinical features and marrow morphology were shown by A.M., but the two tabulated counts were 25 and 2%. The excessive iron stores and hyperferræmia of idiopathic hæmochromatosis (Case Bu.) did not cause an abnormal sideroblast count.

Table VI shows the marrow sideroblast counts and blood sider*ocyte* counts from three patients who had previously undergone splenectomy, and from nine other persons selected because of their higher than average sideroblast counts. The highest siderocyte counts occurred in the two instances where the spleen was absent and the sideroblast counts were high (Hup. and the first count from G.Cl.). With one exception (Case A.W.) siderocyte counts above 11% did not occur in the presence of an intact spleen. Possibly the rapid erythrocyte production rate in Case A.W. caused the high proportion of circulating siderocytes (19% of erythrocytes), assuming that the life span of those cells free of stainable iron granules was reduced by a greater fraction than was that of her short-lived siderocytes. It may be that the survival period of the latter was longer than usual in this case because the inclusions were solitary and small[3] by comparison with the mean inclusion body size in megaloblastic anæmias, thalassæmia and idiopathic erythræmic myelosis. Very few of her normoblastic or erythrocytic granules were visible in Wright's stained preparations. Splenectomy did not give rise to high siderocyte counts in the two instances (R.D., and the second count from G.Cl.) where few normoblasts contained stainable iron granules.

DISCUSSION

The large differences between the mean sideroblast counts of some of the diseases studied were considered to be significant, although the actual mean proportions might not be reproduced by other observers. The intracellular stainable iron granules varied in size from forms that were just visible to forms approximately two microns in diameter. Cytoplasmic granules of varying

Canad. M. A. J.
Mar. 15, 1955, vol. 72

TABLE VI.

BLOOD SIDEROCYTE COUNTS AND MARROW SIDEROBLAST COUNTS WITH AND WITHOUT SPLENECTOMY

Name	*Diagnosis*	*Splenectomy*	*Marrow sideroblasts (% of late nucleated red cells)*	*Blood siderocytes (% of total erythrocytes)*
G.Cl.	Megaloblastic anæmia and total gastrectomy	+	81	32
G.Cl.	29 days after starting vitamin B_{12}	+	2	4
Hup.	Megaloblastic anæmia and partial gastrectomy	+	85	20
A.W.	Acquired hæmolytic anæmia of unknown cause	0	68	19
N.McM.	Idiopathic erythræmic myelosis	0	83*	11*
S.D.	Thalassæmia	0	95	8
E.Cl.	Functionally "aplastic" anæmia (idiopathic)	0	63	7
F.B.	Idiopathic erythræmic myelosis	0	82	5
F.McC.	Pernicious anæmia of pregnancy	0	67	3
Q.F.	Normal	0	24	1
R.D.	Acquired hæmolytic anæmia; portal cirrhosis; blood loss	+	5	1
C.N.	Pernicious anæmia	0	51	0
M.B.	Mild anæmia of unknown cause	0	42	0

*18 months later he had 84% sideroblasts and 2% siderocytes.

shades between black and blue were seen in the iron stained preparations. In examining some preparations, difficulty was encountered in differentiating intracellular siderotic granules of normoblasts from displaced hæmosiderin granules originating in smudged reticulum cells. In the classification of normoblasts by several observers, differences of opinion as to the required size, colour and position of the associated granules would be unavoidable.

In the data reported above, no instance of anæmia due to hypoferræmia (with or without contributory causes) occurred where the marrow sideroblast count was greater than 14%. The anæmia of R.S. (Table III) was considered to be an exception to this statement until more prolonged study indicated that the hypoferræmia was no longer present at an interval after saccharated iron oxide therapy, when the hæmoglobin concentration had dropped back to its pretherapy level. The findings in Tables II and III suggested that low sideroblast counts reflected more than average economy in the use of iron by erythroid cells, although such counts were not invariably associated with hypoferræmia.

Sideroblast counts above 50% occurred regularly in pernicious anæmia, related megaloblastic anæmias, thalassæmia and in two cases of idiopathic erythræmic myelosis. The same group of anæmias also showed higher stainable iron gradings in the marrow reticulo-endothelial cells than would be expected as a result of the iron shift from the diminished erythrocyte compartment.[11] The findings suggested that these conditions shared a similar disturbance of iron utilization for hæmoglobin formation. Lead poisoning might be added to this group because of the high sideroblast counts that resulted from it.[7] Hæmosiderosis and erythrocytic inclusions have been reported in pyridoxine deficient anæmic swine,[17] but there were no data to indicate the presence of iron in the inclusions. The hæmosiderosis of the liver and other organs in thalassæmia[18] may be a more chronic expression of the disorder of iron utilization shared by the diseases with uniformly high sideroblast counts.

For the purpose of this report the term idiopathic erythræmic myelosis was used to indicate an anæmia of unknown etiology associated with extreme erythroid hyperplasia and striking immaturity of the majority of erythroid cells. Impressive reticulocytosis or evidence of hereditary transmission disqualified this diagnosis. The patient described by Pappenheimer[2] with chronic anæmia of unknown cause showing numerous circulating siderocytes after splenectomy may have had the same disease as the two cases listed above as idiopathic erythræmic myelosis.* Hypochromic erythrocytes were observed in blood smears from all three cases. The bone marrow findings were not reported in Pappenheimer's case. A recently reported case of hypochromic anæmia of long duration with secondary hæmochromatosis (not attributable to blood transfusion) may have been one of the same disease.[19] It was of interest that one case of idiopathic erythroid hyperplasia with polycythæmia (F.E. from Table V) did not show an elevated sidero-

*These two cases will be reported in greater detail by Dr. Harold C. Read.

blast count. The adequate function of this patient's erythroid tissue was indicated by her polycythæmia, so that impairment in the utilization of iron was not expected.

Hyperferræmia was observed in case F.B., and saturation of the iron binding protein in both cases of idiopathic erythræmic myelosis. These findings may occur in some other types of anæmia in the absence of greatly increased iron stores. Observations on case E.Cl. (functionally "aplastic" anæmia—idiopathic) indicated the importance of impaired erythropoiesis among the factors responsible for these biochemical abnormalities, and demonstrated the lability of the serum iron level after the total body iron was raised to three times its normal value. One year after the tabulated data on E.Cl. (Table V) were obtained, he had received a total of 19,000 ml. of transfused blood (9.5 gm. iron). The serum iron level was 273 μg. % with saturation of the iron binding protein. A striking temporary remission of his chronic anæmia, neutropenia and debility followed a course of nitrogen mustard therapy,* and the serum iron level fell to 98 μg. % with a total iron binding capacity of 253 μg. %. Data from Case A.M. (Table V) demonstrated that hyperferræmia was not necessarily dependent on the disorder mediating high sideroblast counts where the iron stores were not greatly increased. His anæmia was associated with clinical findings very similar to those of E.Cl., but he was estimated to have half as much iron in the body storage depots at the time when the serum iron level was 209 μg. % (with saturation of the iron binding protein), and the sideroblast count was 2%.

Blood siderocyte counts in four cases of megaloblastic anæmia are listed in Table VI, but high counts occurred only in the two previously subjected to splenectomy. These findings suggested that in megaloblastic anæmias the spleen was concerned with the selective removal of circulating siderocytes. There is evidence that the spleen has an identical role in the anæmias of lead poisoning[7] and in cases of acquired hæmolytic anæmia with high sideroblast counts.[3] It seemed likely that in the two cases of post-gastrectomy megaloblastic anæmia (Hup. and G.Cl.) close to 20 and 30% respectively of the circulating erythrocytes would have been absent in the presence of an intact spleen. It should be noted, however, that other mechanisms for premature erythrocyte removal from the blood, and an impairment of erythrocyte production, are frequently operative in anæmias with high sideroblast counts. Splenectomy was not beneficial in the case of chronic anæmia reported by Pappenheimer,[2] or in two similar familial cases,[5] and has given varying results in thalassæmia.[18]

The ratio of the siderocyte fraction of erythrocytes to the sideroblast fraction of nucleated forms after splenectomy in post-gastrectomy megaloblastic anæmia was approximately 0.3. Other data suggested that with an intact spleen circulating erythrocytes showing visible siderotic granules were permitted only brief survival. Using the observed ratio, one could calculate that a normal person with a sideroblast count of 40% would have 12% less circulating red cells than he would have a few months after splenectomy. This seemed unlikely and suggested that the ratio after splenectomy in otherwise normal persons would be less than 0.3. The data of McFadzean and Davis[3, 7] indicated that this ratio was not fixed because it varied from 0.25 to 0.80 following splenectomy in the abnormal conditions studied by them with Leishman stained preparations.

*Dr. Harold C. Read, who supervised this patient's care, will report the case in greater detail.

SUMMARY

Erythrocytes from blood and orthochromic nucleated red cells from marrow were examined to determine the frequency with which stainable ferric iron particles occurred within these cells in various conditions. The numerical data obtained were correlated with the clinical and hæmatological findings in each case, with the serum iron level and with the stainable iron content of the marrow reticulo-endothelial cells. The latter was used with some reservation as an index of body iron stores.

The proportion of affected normoblasts was regularly low in anæmias due, at least partially, to chronic hypoferræmia, the paucity of affected cells suggesting more than average economy in the use of iron by erythroid marrow cells.

The proportion of affected nucleated red cells was regularly high in pernicious anæmia and related megaloblastic anæmias, thalassæmia and idiopathic erythræmic myelosis. This finding and other evidence suggested that these conditions shared a similar disturbance of iron utilization for hæmoglobin formation.

The largest proportion of affected erythrocytes was observed following splenectomy in patients with a large proportion of affected erythroid marrow cells, indicating that the intracellular iron particles of erythrocytes were deposited in their precursors and that the intact spleen selectively removed affected erythrocytes from the circulation. Other mechanisms for premature erythrocyte removal from the blood and an impairment of erythrocyte production are frequently operative in anæmias with a large proportion of affected erythroid cells, so the effect of splenectomy has been inconsistent in this group. The variable ratio of the affected fraction of erythrocytes to the affected fraction of normoblasts after splenectomy would also contribute to this inconsistency.

Impaired erythropoiesis was the major factor in causing hyperferræmia and saturation of the iron binding protein in two patients.

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EXCISIONAL SURGERY IN PULMONARY TUBERCULOSIS

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SINCE THE EARLY OBSERVATIONS of D'Esopo and associates (1949) a great amount of clinical material has accumulated indicating the questionable viability on culture and guinea-pig inoculation of tubercle bacilli recovered from resected closed lesions of patients treated by chemotherapy. Experience has proved that in open cases combined chemotherapy prolonged over eight months to the so-called "target point" (namely, cavity closure, sputum negative by culture, stable-appearing x-ray film) the same questionable viability of tubercle bacilli arises. One can go further and state that in a high percentage of far advanced cases the same status of questionable viability of tubercle bacilli can be reached if chemotherapy is further prolonged to over 12 months, even if the x-ray film continues to show evidence of large areas of caseous necrosis, open cavities or even destroyed lobes or lungs. At present, the interpretation of these interesting bacteriological findings is controversial. Opinion is divided between those who question viability and those who maintain that our present bacteriological techniques are simply insufficient to demonstrate viability of tubercle bacilli inhibited by chemotherapy.

In considering the foregoing remarks, the practical problem which arises is whether or not we should operate on those cases—perhaps the majority—in which exudative processes clear up and quite often cavitary lesions close, in which negative sputum develops not only on concentrate but also on culture, but in which there is still radiological evidence of more or less large areas of parenchymal necrosis, collapse or destruction. It is frequently noted that clinically these cases have recovered amazingly well. Cough and bronchial secretion are almost nil even in the presence of bronchiectatic changes. The bronchoscopic picture is a non-specific one in that there is œdema, mild inflammation and some degree of stenosis, but there is no tubercle

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formation or ulceration. The blood picture and weight may be extremely good. The problem which we face is that of deciding whether such patients should be discharged or subjected to operation.

Many of us entrusted with the care of tuberculous patients appreciate and are intensely interested in the strong current of clinico-bacteriological studies aiming to assess the pathogenicity, virulence and reproductive properties of tubercle bacilli deteriorated and arrested by bacteriostatic and bactericidal therapy. We believe that the final results may change present-day thought about the surgical management of tuberculous cases. However, until such results materialize, our problem must be approached on practical grounds. The practical points which we must be prepared to answer are the following: What is the present surgical risk of pulmonary resection? In other words, what are the mortality and morbidity? Do the rates warrant the present programme of resectional therapy for pulmonary tuberculosis? Are we justified in advising resection in a patient with "arrested" or sometimes "inactive" disease? It is the purpose of this paper to answer these questions on the basis of our experience with a series of 135 consecutive pulmonary resections, centering our attention on the surgical risk of this procedure. Our criteria in the selection of cases, the radiological findings, chemotherapy, operative indications, type of surgery, mortality and morbidity will be analyzed. An attempt will be made to discuss the technical points which in our experience were basic in securing our results.

Clinical Material

The clinical material reported here consists of cases from the three sanatoria of the Saskatchewan Anti-Tuberculosis League.* The surgery was carried out at the Saskatoon Sanatorium, the League's main surgical centre, between October 1952 and June 1954.

The Selection of Cases

The patients of the three sanatoria are regularly assessed at weekly medical staff conferences. One of the surgeons of the League periodically visits the other sanatoria to discuss possible cases for operation. The patients selected for surgery are admitted to our surgical unit in Saskatoon, where they are thoroughly studied and reassessed. In our service, particular emphasis is given to the radiological study of the patient from the onset of the disease, and the findings are correlated with clinical, laboratory and chemotherapeutic data. We obtain invaluable information from lateral tomography and bronchography as to extension and location of the disease and condition of the contralateral side and the bronchial tree. In the surgical assessment, bronchoscopy and cardio-respiratory tests are always performed. Bronchospirometry is done whenever necessary. For cases with positive culture, sensitivity to antituberculous drugs is determined. Some three or four weeks are spent in the pre-operative study of each case before it is presented to a medico-surgical conference with definite recommendations as to surgery.

General Criteria

1. Resection should be carried out when the body defences are fully mobilized and the general condition is as good as possible.
2. All exudative components of the pathological process should be cleared on chemotherapy and bed rest before surgery. We strongly advocate the principle of maximum resolution of the disease before operation.
3. Cases considered for excision must have at least six months of chemotherapy. The exceptions in this series were rare. Whenever the pathological process is unstable but shows a favourable clinical and radiological tendency, chemotherapy is prolonged up to one year or more.
4. Bilateral cavitary disease was not considered a contraindication to resection if the other side proved to be stabilized for a number of months.
5. Active submucosal or ulcerative endobronchitis was considered a definite contraindication to immediate surgery, but mild reddening of the mucosa was not.
6. Age. In the early part of our series we set up an age limit of 45 years, but soon realized that older patients did surprisingly well. Recently we have accepted for operation patients over 50, some 60 years old, and we have reached the conclusion that the physiological age is more important than the chronological.

Age, Sex, Race

A total of 135 pulmonary resections in 135 patients was performed at Saskatoon Sanatorium from October 1952 to June 1954. The age, sex and racial distribution are grouped in Table I.

Seventy-one per cent of the cases in this series were white and 29% were Indians. The high Indian incidence is noteworthy when one considers that the Indian population in Saskatchewan constitutes approximately 2% of the total population. This particular racial distribution also explains the high incidence of far advanced cases.

*The Saskatchewan Anti-Tuberculosis League has three sanatoria at Fort Qu'Appelle, Saskatoon and Prince Albert, with a total of 800 beds.

TABLE I.

AGE, SEX AND RACE DISTRIBUTION IN 135 PATIENTS

Age			*Sex*			*Race*		
Age	*Cases*	*Percentage*	*Sex*	*Cases*	*Percentage*	*Race*	*Cases*	*Percentage*
Under 10	1	0.7	Female	70	51.1	White	96	71.1
10 to 20	17	12.6	Male	65	48.9	Non-white	39	28.9
21 to 30	63	46.6						
31 to 45	41	30.3						
Over 45	13	9.6						

TABLE II.

CLASSIFICATION AND DURATION OF THE DISEASE IN 135 PATIENTS

C.T.A. classification			*Duration of disease*		
	Cases	*Percentage*	*Years*	*Cases*	*Percentage*
Minimal	9	6.6	1 to 2	55	40.8
Moderately advanced	43	31.8	2 to 5	43	31.9
Far advanced	78	57.7	5 to 10	21	15.5
Non-tuberculous	5	3.7	over 10	16	11.8
Unilateral	40	29.7			
Bilateral	95	70.3			

TABLE III.

SPUTUM BACTERIOLOGY AND ENDOBRONCHIAL DISEASE IN 135 PATIENTS

Sputum bacteriology				*Endobronchial disease*		
Time	*Sputum*	*Cases*	*Percentage*	*T.B. Endobronchitis*	*Cases*	*Percentage*
Admission	Positive	118	87.4	Present	101	74.8
	Negative	17	12.6	Absent	34	25.2
Pre-surgery	Positive	47	34.8			
	Negative	88	65.2			

Table II groups the patients according to the Canadian Tuberculosis Association (C.T.A.) classification and duration of the disease.

Pathological examination proved five cases to be non-tuberculous (one cavitated hydatid cyst, one unresolved chronic abscess and bronchiectasis, three bronchiectasis in collapsed lobes). All were tuberculin-positive.

SPUTUM BACTERIOLOGY

As shown in Table III, 88% of our patients in this series were initially sputum-positive either on concentrate or on culture, but at the time of surgery only 34.8% were still positive. Seven tuberculomatous lesions, five fibroproductive processes and five non-tuberculous conditions account for the 17 initially sputum-negative cases. A radiological-bacteriological correlation with reference to duration and regimen of chemotherapy has been made, and will be the subject of a separate report.

Endobronchial disease, found either by bronchoscopy or bronchography, was present in 74.8% of the cases.

Concurrent disease was discovered in 24 patients. Eight had diabetes and the others had cardiovascular–renal, genital, gastrointestinal and osseous conditions.

TREATMENT PRIOR TO RESECTION

Table IV groups the patients according to special treatment received before resection. About one-half had chemotherapy only, while the others had some form of collapse measure plus chemotherapy.

TABLE IV.

COLLAPSE MEASURES BEFORE RESECTION IN 82 OF THE 135 PATIENTS

Form of collapse	*Cases*	*Percentage*
Pneumothorax	24	17.7
Pneumoperitoneum	36	26.6
Phrenic operations	8	5.9
Thoracoplasty	14	10.3

Fifty-nine patients, about 44% of this series, represent failure of thoracoplasty or other form of collapse. In two, resection failed and was complicated by empyema and bronchopleural fistula. One had a Monaldi procedure.

CHEMOTHERAPY

No attempt will be made to give details of the regimen of drugs and duration in months of treatment. Usually the regimen was streptomycin (SM), one gram every three days or biweekly, with para-aminosalicylic acid (PAS), 12 gm. daily. Isonicotinic acid hydrazide (INH), 300 mgm. daily, was added to or substituted for one of the drugs whenever the result of the treatment was not satisfactory or resistance to streptomycin was encountered. The earlier cases had irregular courses of streptomycin, but recently patients have been on continuous chemotherapy from six months to one year.

RESISTANCE STATUS

This was determined as much as possible during treatment and also immediately before operation whenever positive cultures could be obtained. It is well known that patients having irregular courses of chemotherapy develop drug resistance. Over 25% of our cases were resistant to one or two drugs, but we have reason to believe that the percentage must have been much higher, because in many cases we had positive concentrates but were not able to grow tubercle bacilli.

TYPES OF LESIONS

An attempt has been made to classify the type of lesion by following each case through the whole series of radiographs from the onset of the disease to the time of operation. The main feature of the pathological process was the basis for our classification. A patient having at any time a cavity proved by tomograms was classified as cavitary. A patient with a fibro-cavitary lesion evolved to a destroyed lobe was classified as destroyed lobe. Undoubtedly such a classification is not completely satisfactory, first of all because individual judgment may vary, and secondly because the pathology of pulmonary tuberculosis is pleomorphic, which makes it difficult to classify cases according to any oversimplified scheme. The purpose of this classification is to attempt to correlate radiological findings, clinical data, and sputum bacteriology with the pathology and bacteriology of the resected specimen.

TABLE V.

RADIOLOGICAL CLASSIFICATION OF TYPE OF LESION IN 135 PATIENTS

Type of lesion	*Cases*	*Percentage*
Tuberculomatous	14	10.4
Fibroproductive	14	10.4
Cavitary	43	31.8
Destroyed lobe	32	23.6
Destroyed lung	20	14.8
Bronchial disease	10	7.3
Empyema and B.P.F.	2	1.5

Thirty-two per cent of our cases had cavitary lesions; over 45% had either destroyed lobes or lungs. Nine cases of bronchiectasis also had collapsed lobes. This gives one an idea of the type of case with which we have been dealing. A correlation was established between the type of lesion and the bacteriology of the sputum following prolonged chemotherapy. Of 97 patients initially sputum positive, who had either cavitary lesions or destroyed lobes and lungs, 47% remained positive to the time of surgery. Gross bronchiectasis in collapsed lobes secondary to primary tuberculosis was seldom associated with positive sputum; however, the Mantoux test, the presence of enlarged calcified lymph nodes and the pathological report confirmed the tuberculous etiology. Of patients with tuberculomatous lesions only five had initially positive sputum.

INDICATIONS FOR RESECTION

With the decreasing mortality and morbidity of excisional surgery, the indications for resection are gradually extending, and we feel that any list of indications has more didactic than practical value; the surgical pathology of pulmonary tuberculosis is almost completely covered. In the present stage of our experience we consider resection not as an alternative to thoracoplasty or to other collapse measures, but as the operation of choice whenever possible. For working purposes we select our cases for resection according to four simple criteria:

1. When chemotherapy and rest, prolonged for a sufficient time (8 months to 1 year or more), fail to close the cavitary lesion.

2. When prolonged chemotherapy and bed rest control the disease up to the "target point"

Canad. M. A. J.
Mar. 15, 1955, vol. 72

(cavity closure, negative sputum and stable x-rays), but large residual necrotic areas (filled-in cavities or originally dense lesions) are evident on radiographs. Experience has long proved that the stress of life and intercurrent disease are precipitating factors of reactivation, particularly in the young patient group, diabetics, alcoholics, the emotionally unstable, non-cooperative patients, racially susceptible patients and the indigents. Under this criterion fall a number of minimal cases of tuberculomatous or fibroproductive lesions, which obviously are so-called borderline cases, where the question of resection arises. For a time we had our doubts, but now feel that the operative risk and morbidity are so insignificant that resection is justified.

3. When patients either represent the failure of collapse measures or show large areas of anatomical and functional destruction of lobes or lungs. Gross bronchiectasis and empyema are included in this group. In these cases prolonged chemotherapy and bed rest are extremely valuable in controlling the contralateral disease, in clearing the acute exudative components of the process, in healing the tuberculous endobronchitis and in improving the general condition of the patient who, from a desperate risk, may be converted to a fair or a good one.

4. When diagnosis cannot be proved, suspicion of tuberculosis remains, and biopsy is necessary.

CONTRAINDICATIONS TO RESECTION

A liberal indication for resection does not exempt one from exercising the greatest care in searching for contraindications to such a radical treatment. Any relaxing of the most critical approach is unjustified and may be responsible for failure. Timing is invaluable in securing the optimum result. Experience proves that the patient who is a desperate surgical risk today often becomes a better risk after another six to eight months of chemotherapy and bed rest.

Definite contraindications to resection are: (1) active ulcerative or submucosal tuberculous endobronchitis at the line of prospective transection of the bronchus; (2) wide-open contralateral cavity, new disease or recent reactivation in the operative or in the contralateral lung; (3) cardiopulmonary insufficiency, and (4) an age limit of about 60, depending on physiological condition. Conditions 1 and 2 are temporary contraindications, being generally controlled by a further course of chemotherapy. Condition 3 cannot be definitely assessed by pulmonary function tests or even by bronchospirometry, for we have been much impressed by the remarkable adjustment and tolerance that patients with massive disease develop after surgery.

TYPE OF RESECTION

Table VI shows that out of 135 resections about 65% were either lobectomies or pneumonectomies. Only 35% had minor resections, wedges or segments.

TABLE VI.

TYPE OF RESECTION IN 135 PATIENTS

Procedure	*Cases*	*Percentage*
Wedge	3	2.3
Segmental	45	33.4
Lobectomy	61	45.2
preceded by TCP 28		
associated TCP 11		
without TCP 22		
Pneumonectomy	4	2.9
Pleuropneumonectomy	22	16.3

The 1953 and 1954 statistics of the Veterans' Administration Group in the U.S.A. show a much higher incidence of segmental resection than of lobectomy and pneumonectomy. This is just the opposite of what we found in our series, for the reason that 89% of our cases were moderately and far advanced. Other explanations are that there was an accumulation of surgical material in our three sanatoria, and that about 30% of our patients were Indians, who unfortunately accept the sanatorium regimen only when they reach an advanced stage of disease; in fact, in 82% of these Indians disease was far advanced and all needed either lobectomy or pneumonectomy.

SEGMENTAL RESECTIONS

In this series 45 segmental resections stand against only three wedge resections. This proportion shows our limited indications for wedge resection and reflects our lack of enthusiasm for this procedure, mainly on surgical and pathological grounds. We share the opinion that, as the bronchus draining the diseased area is inevitably involved by the tuberculous process, it should be removed well proximally, at the level of the primary segmental division, in order to prevent recurrence or complications. Of the 45 segmental resections, 33 involved the apical or

posterior or both segments of the upper lobe, and seven the apical segment of the lower lobe. These figures confirm once again this peculiar segmental distribution of pulmonary tuberculosis as proved by Churchill, Brock, Overholt, Chamberlain and others. The apical segment of the lower lobe was also removed in many upper lobectomies, but these cases are not mentioned under segmental resections. As a rule, resection involving only one or two segments did not require a thoracoplastic space-reducing measure.

LOBECTOMIES

There were 61 lobectomies, 39 on the right and 22 on the left. The upper lobe was removed in 30 cases, the upper and mid lobe or lingula in 14, and the lower lobe or other combinations in 17. Decortication was done with lobectomies in 22 cases. In five cases upper lobectomies did not require thoracoplasty, while in 28 cases lobectomy was preceded by a modified thoracoplasty. In 11 cases lobectomy and thoracoplasty were done in one stage. Lower lobe resection did not require any space-reducing measure. We feel that the usual elevation of the diaphragm following lower lobe resection is satisfactory in this respect. The phrenic nerve was always preserved.

PNEUMONECTOMIES

There were four pneumonectomies and 22 pleuropneumonectomies, a total of about 20% of the entire series. Pleuropneumonectomy has been the procedure of choice whenever total or partial obliteration of the pleural space was encountered. We believe that the more radical pleuropneumonectomy offers fewer complications and better chances for good results. Pneumonectomy was preceded by one or two stages of thoracoplasty. A third stage was always completed at the time of excision. In a few instances pneumonectomy and segmental costectomy—from ribs two to six—were done in one stage. A single case of pneumonectomy did not require thoracoplasty of any kind. Phrenic interruption was done routinely in our pneumonectomy cases.

EVALUATION OF SURGICAL RISK

Surgical or postoperative deaths and complications are those occurring within 60 days of operation. Late deaths and complications are those occurring more than 60 days after operation. Complications are further divided into tuberculous and non-tuberculous. Table VII gives the number of deaths in 135 patients.

TABLE VII.

SURGICAL MORTALITY

Total resections—135	Death—1	Mortality—0.7%
Procedure	*Cases*	*Deaths*	*Percentage*
Segmental and wedge....	48	—	—
Lobectomy.....	61	1	1.6
Pneumonectomy.....	26	—	—

SURGICAL DEATHS

The single death, occurring in the fifth case of the series, was not tuberculous but was due to pulmonary embolism following a right lobectomy. The patient died after operation while being moved from the operating table to his bed. Autopsy showed the presence of a recent pulmonary embolus arising from his left leg. No deaths occurred in the pneumonectomies or in the segmental resections. In this series 130 consecutive resections were performed with no fatality. Surgical difficulties and age did not bear any relation to surgical mortality; in fact, the one death was not related to technical matters.

LATE DEATHS

So far no deaths have been reported. At the time of presentation of this report, about 70% of the patients have a follow-up of from one to two years. The remainder vary from four to 11 months. Such periods are too short to permit reliable conclusions.

COMPLICATIONS

Table VIII gives the whole picture of all tuberculous and non-tuberculous postoperative complications, distributed according to type of surgery.

TUBERCULOUS COMPLICATIONS

As may be seen from Table VII, there were no tuberculous complications in the postoperative period, no empyema, no bronchopleural fistula and no tuberculous spread. Later, an unfavourable trend was noted in two cases.

One developed a tuberculous spread in the contralateral lung followed by diffuse tuberculous endobronchitis, ulceration of the bronchial stump and a small pocket of empyema. The spread appeared four months after pleuropneumonectomy, the ulceration and empyema twelve months after operation. This patient had previ-

Canad. M. A. J.
Mar. 15, 1955, vol. 72

TABLE VIII.

POSTOPERATIVE COMPLICATIONS IN 135 PULMONARY RESECTIONS

Procedure	Tuberculous complications—0			Non-tuberculous—11 (8.1%)			
	Tuberculous			*Non-tuberculous*			
	Empyema	*B.P.F.*	*Spread*	*Wound infection*	*Air leak*	*Delayed expansion*	*Thrombo-phlebitis*
Pneumonectomy	—	—	—	2	—	—	—
Lobectomy	—	—	—	—	—	—	1
Segmental	—	—	—	—	7	1	—

ously undergone multiple-stage thoracoplasty and was resistant to SM and INH. A full course of Viomycin did not improve the condition of the patient and he benefited very little from Pyrazinamide. A dramatic improvement, both clinically and radiologically, was obtained by continuous external suction-drainage of the small empyema pocket. The local treatment consisted of alternate instillation of SM and Varidase. It is interesting to note that while this patient was developing the complications mentioned and was clinically ill, his tubercle bacilli, easily recovered from the sputum, did not grow in cultures and did not infect three guinea-pigs inoculated at monthly intervals. This patient's sputum has remained negative by concentration and culture since April 1954.

The second case developed an intermittently positive sputum five months after resection of the right middle lobe and the anterior segment of the upper lobe. Sputum from the right upper lobe was positive on bronchoscopy. There were no radiological changes. The patient is well and the sputum has been negative for many months.

NON-TUBERCULOUS COMPLICATIONS

The postoperative complication of "air leaks" was confined to segmental resection cases. Seven patients developed spontaneous pneumothorax of the tension type from two to four weeks after uneventful segmental resection. It is remarkable that all had simple procedures followed by quick ideal re-expansion of the remnant lung. No pleural effusion, no temperature, or other heralding symptoms were noted. In three of the seven cases we could blame over-exercise and interruption of postoperative routine; in the other four we have no clues. Pneumothorax was suspected because of sudden chest pain and dry cough. Shortness of breath was noted in two instances, elevation of temperature in the others. A sudden loss of appetite and a feeling of not being well were complaints common to all of them. X-ray films confirmed the presence of pneumothorax. Treatment in all these cases was instituted immediately and consisted of continuous intrapleural suction applied via needle or polyethylene tube inserted through a large bore needle. Re-expansion always occurred within two or three days—sometimes in twenty-four hours. Results have been excellent. In no instance was there infection nor did we need thoracotomy or thoracoplastic measures.

MINOR COMPLICATIONS

The other postoperative non-tuberculous complications were four in number. Two were a pyogenic infection of the subscapular space following pneumonectomy; they cleared rapidly and well on antibiotics. The third was a thrombophlebitis following lobectomy and cleared up on rest and antibiotics. The fourth was a delayed re-expansion resulting in a mild pleural effusion after segmental resection involving two segments of the upper and one segment of the middle lobe. No "air leaks" were discovered. This case did not respond to continuous intrapleural suction. Ultimately he required a two-rib modified thoracoplasty, from which he recovered promptly.

ANÆSTHESIA

There is no other type of surgery where expert administration of the various anæsthetic and relaxant agents combined with skilful management of the anæsthetic procedure is as important as in thoracic surgery. The success of the operation depends equally on the surgical team and on the anæsthetist. All operations were done under general endotracheal anæsthesia. Nitrous oxide-oxygen supplemented by intermittent intravenous thiopentone (Pentothal) in many cases was sufficient to carry out the whole procedure. In others cyclopropane or ether was added as necessary. During surgery the respiration was assisted to prevent accumulation of CO_2. The bronchial tree was intermittently aspirated through the endotracheal tube. In no case was a postoperative bronchoscopy necessary to remove secretions from the bronchial tree. It was our routine to infiltrate the root of the lung and the vagus nerve with 1% procaine at the start of the hilar dissection. There was no instance of cardiac arrest.

POSITION ON THE TABLE

In 135 patients the operation was carried out with the patients lying in a lateral position. We found this position more convenient than the prone, which was indicated only in five cases on account of very low vital capacity or unusually wet bronchiectasis. Incidentally, the single death occurred in one of the prone-position cases and was due to a pulmonary embolus mobilized from the leg when the patient was being moved to the supine position.

MORTALITY

Surgical mortality rates reported in the current literature on resection for pulmonary tuberculosis range from a minimum of about 2% to figures much higher. Figures published in 1953 and 1954 by the Veterans' Administration, U.S.A., may be considered as average. They show the following mortality rates.

TABLE IX.

PERCENTAGE OF SURGICAL MORTALITY FOR PULMONARY RESECTION IN TUBERCULOSIS, VETERANS' ADMINISTRATION, U.S.A., 1953 AND 1954

Procedure	*Percentage of surgical mortality*	
	1953	*1954*
Pneumonectomy	11.0	9.8
Lobectomy	3.1	2.7
Segmental resection	0.4	0.05

The most frequently recorded causes of death in the operating room are hæmorrhage, cardiac arrest, respiratory failure, and shock. Immediate deaths (to 72 hours) are due to hæmorrhage and shock, acute pulmonary œdema, heart failure, pulmonary embolism, pulmonary insufficiency, atelectasis and transfusion incompatibility. Some deaths are preventable; some are unavoidable in spite of the best preparation, surgical technique and anæsthesia. In our series we had three cases of tears of segmental arteries extending on the main pulmonary artery in spite of the most careful dissection. Attempts to expose and reclamp the torn area of the pulmonary artery resulted in an extension of the tear in the proximal direction, leaving less and less tissue for a safe ligation. From experience we learned to control the hæmorrhage by finger pressure, to expose the main pulmonary artery well proximally to the tear and to apply a very soft rubbered clamp, in order to interrupt the blood stream. No time or blood should be wasted in useless and dangerous attempts to control the bleeding by blind clamping. The specimen should be removed in the quickest possible manner, ligating the vessels and clamping the bronchus. After the specimen is removed, there is much more room to expose the torn vessel with gentle dissection and under perfect vision. A ligation or a suture is so feasible in saving the patient's life and possibly a lobe or an entire lung.

COMPLICATIONS

The leading early and late complications following pulmonary resection are bronchopleural fistula (BPF), empyema and spread of disease. The incidence of each of these complications according to current literature varies over a wide range, from a minimum of 5% to a maximum as high as 20% or even 30%. The data reported by the Veterans' Administration, U.S.A., in 1953 and 1954 are condensed in Table X.

BPF AND EMPYEMA

By and large, when a BPF and empyema are established, about 50% of the patients die. In less than 30% does the BPF close after further surgery. The rest carry on life with discharging sinuses. It is common experience that the incidence of bronchopleural fistula and empyema is

TABLE X.

PERCENTAGE OF COMPLICATIONS FOR PULMONARY RESECTION: VETERANS' ADMINISTRATION, U.S.A., 1953 and 1954

Treated with SM or DHSM and PAS	*Percentage of postoperative complications*							
	B.P. fistula		*Empyema*		*Spread*		*Other*	
	1953	*1954*	*1953*	*1954*	*1953*	*1954*	*1953*	*1954*
Pneumonectomy	10	16	8	16	4	8	13	32
Lobectomy, no associated TCP	1	2	1	1	4	1	13	15
Lobectomy with prior TCP	5	9	3	11	2	2	14	6
Lobectomy and concomitant TCP	3	2	2	0	3	0	8	6
Lobectomy and subsequent TCP	11	28	9	23	1	0	9	18
Segmental resection	5	5	2	3	1	1	6	15

Canad. M. A. J.
Mar. 15, 1955, vol. 72

higher with pneumonectomy than with other procedures. This leads one to think that following pneumonectomy there is something wrong with the obliteration of the dead space. In our series we used, as a rule, extensive single or multiple stage thoracoplasty for pneumonectomy, and one stage modified thoracoplasty or limited segmental costectomy for lobectomy and those segmental resections which involve more than two segments.

Other causes which we consider responsible for BPF and empyema are the length of the bronchial stump and its insufficient pleuralization. There is a tendency to leave a long bronchial stump, particularly in pneumonectomy, as we ourselves found, using the opened bronchus suture technique. The shorter the stump, the easier its obliteration between flaps of mediastinal pleura. The ideal pneumonectomy stump sinks deeply into the mediastinum and does not require any pleuralization. Should an empyema develop under these conditions, it would be confined to the pleural space and would not open into the bronchus, thereby greatly reducing the risk of contralateral spread and progressive fatal disease. For pneumonectomy and lobectomy a short stump placed in extrapleural position is usually possible, but for segmental resection this is not technically feasible. In this situation we embed the stump directly into the parenchymal tissue and reconstruct the mediastinal pleura as usual.

CONTAMINATION OF THE PLEURAL SPACE

The contamination of the pleural space with tuberculous material from broken-in cavities or caseous lymph nodes has been blamed for empyema and BPF. In almost all resections for tuberculosis, more or less gross contamination of the pleural space is present at the end of the procedure. Transection and stitching through a diseased bronchus, incomplete removal and sequestration of lung parenchyma or diseased pleura are, we believe, the sources of continuous supply of organisms, with resulting BPF and chronic empyema. Continuous irrigation during surgery and the establishment of an efficient drainage minimize the risk of pleural contamination. It has been our principle to choose the extrapleural cleavage whenever thick adhesions suggest the invasion of the parietal pleura by the disease. Pleuropneumonectomy has been our operation of choice in 22 out of 26 pneumonectomies.

SPREAD OF THE DISEASE

Although this is not as common an occurrence as in the pre-streptomycin era, it stands always as a potential risk if proper precautions are not taken. The timing of surgery, the preparation of the patient, the surgical technique and anæsthesia, and the postoperative management, are all equally responsible. Early clamping and transection of the bronchus has been our technique of choice in the presence of copious bronchial secretion. Overexpansion of a previously diseased area of the lung is dangerous following resection. A modified thoracoplasty, preceding or associated with resection, is used whenever the resected portion of the lung is in excess of the volume of two normal segments.

ATELECTASIS

Atelectasis, whether obstructive, compressive or neurogenic, can be minimized by a combined rational application of the principles enumerated previously. Gentleness, minimal manipulation and damage to the tissues, clean anatomical dissection strictly confined to the portion of the lung to be removed and minimal injury to the surrounding structures are the determining factors of an uneventful postoperative course.

AIR LEAKS

Prolonged leakage of air is commonly encountered in segmental resection. This is probably related to persistent patency of intersegmental bronchioles which were not ligated at the time of operation. Our experience has been peculiar in this respect since our seven cases of air leaks occurred between the 10th and the 20th postoperative day following an uneventful course. We now suspect that in these cases we did not pay enough attention to ligation of the sources of these so-called alveolar leaks, which generally seal off by fibrin deposition and rapid re-expansion of the remnant lung. It is possible that one or two weeks later the marginal atelectasis and alveolar collapse at the intersegmental plane resolve, re-establishing the bronchiolar aeration with air leakage in the free pleural space. The minimal serous pleural reaction which follows is sufficient to seal the leaking points if building up of the intrapleural positive pressure is prevented and re-expansion of the lung encouraged by negative intrapleural suction. Since we started ligating the major air leaks during the operation, we have had no more

of this complication. We may conclude that the prevention of postoperative complications in our experience was based on the following surgical principles: (1) Clean, gentle, meticulous anatomical dissection. (2) Extrapleural cleavage whenever parietal adhesions were found. (3) Obliteration of the dead space. (4) Accurate dissection of the bronchus, with preservation of its blood supply. (5) Shortest possible bronchial stump simply stitched with fine black silk. (6) Accurate reconstruction of the mediastinal pleura over the stump, which results in its being placed extrapleurally in pneumonectomy and lobectomy; direct embedding of the bronchial stump into the parenchymal tissue in segmental resection. (7) Ligation of the major sources of air leaks. (8) Correct placing of the drainage tubes. (9) Rapid re-expansion of the lung remnant after lobectomy and segmental resection. (10) Prevention of over-expansion.

PRESENT POSITION OF 135 RESECTION CASES

Of the 135 patients undergoing resection one died of pulmonary embolism; 134 are living. One has reactivation in the contralateral lung, ulceration of the bronchial stump and a small pocket of empyema. Sputum concentrates, cultures as well as guinea-pig, have been negative since April 1954. One has intermittently positive sputum but is clinically and radiologically well, and the sputum may be converted to negative on prolonged chemotherapy. With the two exceptions, all patients are well, have gained weight and are symptom-free. One hundred and fifteen of the 135 patients have already completed their postoperative routine of six months' sanatorium treatment with chemotherapy and are now discharged. All of the discharged patients are reviewed every three months, are doing well, and are sputum-negative; many of them are already engaged in full- or part-time work.

CONCLUSION

1. Pulmonary tuberculosis remains a medical disease. Well-planned chemotherapy and bed rest are the basic treatments which in the majority of the cases must be prolonged as much as eight to twelve months before any decision is made about surgical interference.

2. Excisional surgery has a definite place in the treatment of pulmonary tuberculosis. The indications are gradually extending and our trend is towards replacement of thoracoplasty by excision.

3. The procedure is safe provided the indications for it are fulfilled. Mortality and morbidity are very low if sound criteria in selection of cases, timing of operation, pre- and postoperative management and meticulous surgical techniques are observed. There is no place for a standard operation or a routine postoperative management. Each case must be approached and studied as an individual problem.

4. This series of 135 consecutive pulmonary resections has been extremely encouraging, with a total mortality rate of 0.7% and a very low morbidity rate.

5. In our limited experience, the mortality encountered in segmental resection for removal of small dense lesions has been nil and the few complications have been insignificant. From the risk point of view, it is felt that the present programme of resectional therapy in pulmonary tuberculosis is justified and we are encouraged to continue our surgical attack on residual necrotic foci. If resection does not cause any more risk than appendectomy, we are inclined to remove the destroyed areas of the lung containing viable or questionably viable bacilli, but definitely containing tubercle bacilli, which represent a threat to life. We recall our case of spread of the disease by tubercle bacilli which were non-viable on culture and guinea-pig inoculation.

6. We do not know the ultimate results, but for the present they compare favourably with those obtained by collapse measures and chemotherapy.

SUMMARY

1. Chemotherapy has revolutionized the former concepts of clinical pathology, bacteriology and treatment of pulmonary tuberculosis. In the majority of cases, prolonged chemotherapy controls the disease up to the stage of being "arrested" or "inactive." Tubercle bacilli recovered from resected lesions show questionable viability in culture as well as in guinea-pig inoculation. The question arises whether excision is needed and what is the risk.

2. A personal series of 135 pulmonary resections for tuberculosis is presented—26 pneumonectomies, 61 lobectomies, and 48 segmental resections.

3. The selection of cases, statistical analysis, sputum bacteriology, endobronchial disease, treatment before resection, type of lesions, indication and type of resection, surgical mortality and complications are discussed.

4. In this series there has been but a single death and this was due to pulmonary embolism. The operative death rate is 0.7%. No late deaths have been reported with a follow-up from three to 24 months. The total complication rate has been 8.1%.

5. The present position of the patients is reviewed.

6. The surgical points which in the author's experience were basic in securing the results are discussed.

It is a pleasure to acknowledge the valuable assistance of Dr. J. Orr, Director of the Medical Services of the Saskatchewan Anti-Tuberculosis League, in the preparation of this study and in giving permission to publish it. Grateful thanks are due to the superintendents, surgical assistants, and medical, laboratory and x-ray staff of the three sanatoria for the full co-operation we have been given throughout.

We are also indebted to Dr. J. W. Adams, pathologist of the City Hospital, for pathological examination and report on all our resected specimens.

ADDENDUM: At the time of publication of this paper 168 consecutive resections have been performed without fatality.

NOTE—A comprehensive list of 55 references has been prepared and may be obtained from the author on request.

Saskatoon Sanatorium.

RÉSUMÉ

1. La thérapie chimio-antibiotique a révolutionée les anciennes conceptions de la pathologie, de la bactériologie et du traitement de la tuberculose pulmonaire. Dans la majorité des cas la chimiothérapie de longue durée conduit la maladie jusqu'au stage "d'arrêt" ou "d'inactivité". Les bacilles tuberculeux prélevés des spécimens opératoires démontrent une incertain capacité de se réproduire dans les cultures et d'infecter les cobayes inoculés. On se demand si la résection est nécessaire et quels en sont les risques.

2. On rapporte une série personnelle de 135 résections pulmonaires pour tuberculose, 26 pneumonectomies, 61 lobectomies et 48 résections segmentaires en les analysant selon la bactériologie du crachat, le caractère des lésions, le traitement avant la résection, l'indication et le type de résection, la mortalité et les complications opératoires.

3. Dans cette série la mortalité opératoire a été de 0.7%, le seul décès ayant été causé par une embolie pulmonaire. On ne déplore aucun cas de décès tardif, après un contrôle clinique de 3 jusqu'à 22 mois. Le pourcentage des complications a été de 8.1%.

4. On décrit la condition présente des malades et on discute certains points de téchnique chirurgicale que l'auteur considère comme capitaux. F.F.A.

AN OUTBREAK OF PARALYTIC SHELLFISH POISONING

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PARALYTIC SHELLFISH POISONING was first recognized as a public health problem on the Atlantic Coast of Canada in 1936, when Murphy[1] reported that five cases with two deaths had occurred in Nova Scotia following the consumption of mussels. Other investigations revealed a serious problem,[2] and since 1943 collaborative studies have been conducted without interruption by the Department of National Health and Welfare, the Department of Fisheries, and the Fisheries Research Board of Canada. In 1947, Medcof *et al.*[3] presented a comprehensive report of an epidemiological study in which the toxicity of raw shellfish, the dosage of poison, and the resulting symptoms were correlated. They showed that the mildest symptoms of poisoning were observed only when a quantity of poison in excess of 1,000 mouse units was ingested, thus confirming the 400 mouse unit quarantine level first suggested by the work of Sommer and Meyer.[4] The clinical picture in the 28 human cases in New Brunswick in 1945 was carefully studied. The symptoms varied in severity with the amount of poison ingested, but were consistent: numbness about face and mouth, with paræsthesiæ of the lips; vomiting; headache; dizziness; difficulty in breathing; general weakness; occasional paralysis. Poisoning of domestic animals, particularly house cats, seems to have been common. A traditional knowledge of the dangers involved, and a degree of resistance to the poison, apparently have prevented more frequent illness among the inhab-

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itants of shore communities; many instances of shellfish poisoning have been reported among tourists and other visitors to the fishing areas for whom shellfish were not a habitual item of diet.

Medcof *et al.* concluded that the minimum amounts of poison required to produce mild, severe, and extreme symptoms of poisoning in susceptible persons might be in the neighbourhood of 2,000, 10,000 and 25,000 mouse units respectively. Domestic cooking processes, including steaming and pan-frying, were found to reduce the poison content of raw clam meats by at least 70%, but failed to provide sufficient protection in many cases.

Gonyaulax tamarensis, a species of dinoflagellate on which shellfish feed, has been shown to be the ultimate source of the poison.[3] A close correlation between large numbers of the dinoflagellate in seawater and the appearance of high toxicities in shellfish has been observed, usually between mid-July and the end of September on the Canadian Atlantic coast. All of the molluscan shellfish found in the Bay of Fundy have been shown to be toxic to some degree at such times; the soft-shell clam (*Mya arenaria*) is the most important commercial species and, fortunately, is the least dangerous (oysters are not found in the Fundy area, and as a species have never been shown to be toxic). Since 1943 the Department of Fisheries, on recommendation from the Department of National Health and Welfare, has imposed temporary restrictions on the taking of shellfish from toxic areas in New Brunswick; at such times the clam beds have been closed to all fishing except for canning. All canned packs from toxic areas are routinely checked for toxicity before release. Dangerous areas have been posted with warning signs. There has been no difficulty in maintaining a reliable control over all commercial operations, but it has not been easy to enforce the fishing prohibition on the general public.

A shellfish toxicity problem has also been known to exist on the south shore of the St. Lawrence River since 1948, when two children died from eating what are believed to have been mussels (*Mytilus edulis*) collected at Les Boules, Que.[5] The recent discovery of large stocks of soft shell clams on the north shore of the St. Lawrence has stimulated interest in the toxicity problem and its effect on possible commercial exploitation of the clams. Since 1953 the Department of Fisheries of the Province of Quebec, in close co-operation with the Department of National Health and Welfare, has adopted control measures virtually the same as those employed in the regulation of the clam fishing industry in New Brunswick and Nova Scotia. Extracts from clam specimens taken periodically from producing areas on both shores of the St. Lawrence River are tested for toxicity at the Laboratory of Hygiene, Ottawa; when toxicity values reach the quarantine level of 400 mouse units, the areas are closed to commercial fishing and warning signs are posted on the beaches. Nearly 550 specimens of Quebec clams have been tested for toxicity since March 1953.

On July 6, 1954, a routine toxicity test indicated that soft-shell clams from Metis Beach on the south shore of the St. Lawrence River contained 419 mouse units of toxin, and the area was closed to fishing. A family of seven persons (the parents, Mr. and Mrs. A.G., a daughter-in-law, Mrs. R.G., a son, R.G., and three daughters, Mrs. R., Miss C.G., and Miss D.G.), visited Metis Beach, and on July 13 collected mussels (*Mytilus edulis*) from the beach. C.G. ate two or three mussels without ill effect; R.G. consumed an undetermined number of mussels and suffered from "upset digestion," while his wife, Mrs. R.G., who ingested a somewhat larger number of mussels, complained of stomach cramps and violent diarrhœa. The family cat ate an undetermined number of mussels, with subsequent paralysis and disturbed head movements. On July 14 all members of the family except Mrs. R. ate an indeterminate number of mussels collected at St. Flavie, P.Q., without ill effect.

On July 15, between 9:00 and 10:00 a.m., soft-shell clams were collected from the Metis Beach tidal flats. Although the G. family was informed of the danger from shellfish poison by residents of the area and by warning signs on the beach, the clams were steamed and eaten between 11:00 a.m. and 12:00 noon. No clam bouillon was ingested. Symptoms appeared within one-half hour after ingestion of the clams, and were the same in all members of the family (see Table I). The family cat refused to eat the clams and was not affected. All patients except Mrs. R. were induced to vomit within one hour after ingestion of the clams. Mrs. R. died at 12:45 p.m. and Mr. R.G. at 3:00 p.m. July 15. The others recovered by July 17, and were discharged from Rimouski Hospital on July 22.

TABLE I.

	Symptoms						
	Mr. R.G.	*Mrs. R.*	*Mr. A.G.*	*Mrs. A.G.*	*Mrs. R.G.*	*Miss C.G.*	*Miss D.G.*
Age	36		69	60	34	27	12
Clams ingested	32–40	12–15	12–15	5–6	5–6	3–4	3–4
Minimum weight (gm.)	326.7	122.5	122.5	51.1	51.1	30.6	30.6
Maximum weight (gm.)	408.4	153.2	153.2	61.3	61.3	40.8	40.8
Paræsthesiæ (lips)	yes	yes	yes	yes	yes	yes	yes
Occipital headache			yes			yes	
Vomiting	yes	nausea	yes	yes	yes	yes	yes
Paralysis	yes	yes	yes	yes	yes	yes	yes
Apathy			yes	yes	yes	yes	yes

Field Investigation

Two of the authors (J.N. and H.E.C.) established a sampling station at the point on the Metis Beach tidal flats where clams had been collected by the G. family; specimens of *Mya arenaria* were collected daily from this point from July 18 to July 22. Extracts were prepared as follows: the clams were shucked, washed in fresh water, drained on a sieve for 5 minutes, and thoroughly minced; a 100-gram portion of the minced meats was suspended in 100 ml. of 0.1 N hydrochloric acid, and boiled gently for 5 minutes with continuous stirring; the mixture was then cooled, made up to its original volume (200 ml. approximately) with distilled water, and the pH adjusted to between 4.0 and 4.5 by addition of a few drops of 5N acid or 0.1 N sodium hydroxide, using B.D.H. universal indicator internally. The supernatant liquid was clarified by settling, and constituted the extract which was shipped to the Laboratory of Hygiene for assay.

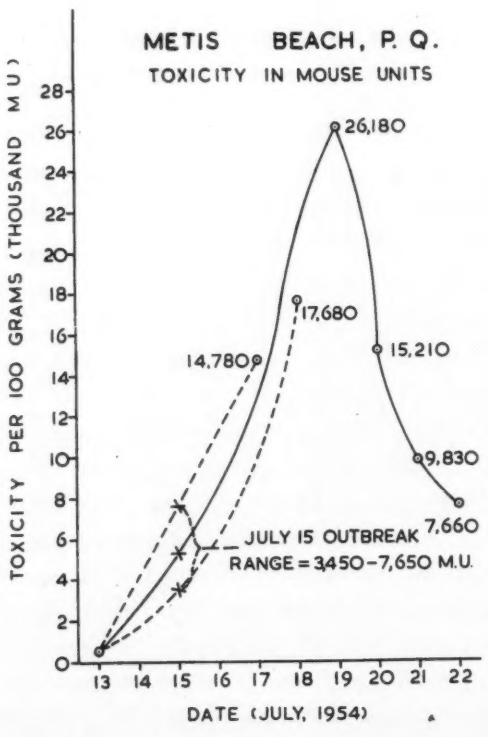

Fig. 1

One millilitre of the extract (and decimal dilutions) was injected intraperitoneally into each of three white mice (18 to 22 gm.), and their death times were measured to the nearest five seconds. The mean death time was referred to a standard toxicity graph from which toxicity was determined and expressed as "mouse units." All toxicities for *Mya arenaria* taken from Metis Beach during the study period are tabulated below, and are plotted on a graph (Fig. 1).

TABLE II.

Date	*Toxicity*	*Date*	*Toxicity*
July 13	542	July 20	15,210
July 17	14,780	July 21	9,830
July 18	17,680	July 22	7,660
July 19	26,180		

Replicate clam specimens from Metis Beach were shucked and weighed; the mean weight per clam was 10.21 gm.

Since no specimens were obtained from Metis Beach on July 14, 15 and 16, only a rough approximation of the probable toxicity level on July 15 can be obtained by interpolation on the graph. It is probable, however, that the clams eaten by the G. family contained from 3,450 to 7,650 mouse units per 100 gm. of meat.

Medcof *et al.*[3] concluded that steaming reduces the poison content of clam meats by at least 70%. Dosages were therefore calculated on the basis of the approximate level of toxicity in Metis Beach clams on July 15, and on the assumption that 30% of the poison remained after steaming. Dosages were also calculated for 100% retention of the toxin during steaming, to provide an estimate of the maximum possible dosage.

Conclusions

Because insufficient information is available, no very precise measure can be made of the dosages of shellfish poison which produced illness and two deaths in the seven members of one family. It is impossible to determine the exact poison content of the ingested clams, and the precise

effect of steaming on their toxin content. It is evident, however, that one death (R.G.) resulted from the ingestion of not less than 3,300 mouse units, and not more than 31,300 m.u.; if the loss of toxin due to steaming was approximately 70%, it is probable that approximately 5,800 m.u. of shellfish poison were ingested by R.G.

The second fatality (Mrs. R.) resulted from the ingestion of not less than 1,200 m.u., and not more than 11,700 m.u.; a dosage of approximately 2,400 m.u. is considered to be probable. A.G. survived a similar dosage; it is probable, therefore, that the dosage in Mrs. R's case approached the minimum lethal dose.

Mrs. A.G. and Mrs. R.G. ingested not less than 528 m.u. and not more than 4,700 m.u. (probably about 1,000 m.u.). Misses C.G. and D.G. ingested not less than 300 units and not more than 3,200 m.u. (probably about 650 m.u.).

The unfortunate outbreak of paralytic shellfish poisoning reported herein points up the need for continued rigid control of clam-producing areas. Clams with toxicities of 400 mouse units or more per 100 gm. of meat must be excluded from the market at all times.

The persons involved in the Metis Beach outbreak collected and ate the toxic clams in spite of what should have been adequate warning from local residents and from signs posted on the beaches. It may be necessary to take further measures for the protection of tourists unfamiliar with the shellfish toxicity problem.

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THE PRACTICAL TESTING OF VESTIBULAR LESIONS*

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IN ORDER to determine the origin of vertigo it is essential, in addition to taking an accurate history, to have reliable test procedures. If the vertigo is due to an end-organ lesion, the patient recognizes at once the similarity of his attacks and the rotational vertigo artificially produced by clinical testing. Furthermore, by the use of unilateral stimulation each organ of balance can be tested separately, thereby providing significant information as to the side and the site of the lesion. The prompt recognition of this type of vertigo produced by peripheral stimulation is most significant since it differs from that due to central irritation.

Following the testing of over 200 consecutive patients referred for investigation of vertigo at St. Michael's Hospital, it appears evident that certain vestibular tests are of particular value. It is the purpose of this paper to suggest a routine procedure which has been found to be most practical.

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PROCEDURES

One of the most reliable of tests that can be carried out in the doctor's office is the *caloric test*. By raising or lowering the temperature of the petrous bone with the application of heat or cold to the ear drum, the fluid in the adjacent lateral semi-circular canal is induced to flow by convection currents. One simple method is to introduce 5 c.c. of ice water into the ear canal by means of a 10 c.c. syringe and needle of moderately small calibre, with the patient sitting up or in the prone position. The direction (quick phase) and duration of the nystagmus produced are then recorded. Normally with cold water (lower than body temperature) the quick phase beats to the opposite side; this should be reversed by warm water. After a few trials on normal patients, the physician can evaluate the hyperactive or hypoactive end-organ responses. Nystagmus produced in this fashion normally lasts two minutes. This procedure is highly recommended by McNally.[1] The interpretation of these responses will be discussed later.

Another caloric test which we have used more frequently than the above is the method of Fitzgerald and Hallpike.[2] This procedure has the advantage of greater accuracy, since the stimulus is more within physiological limits and consequently less disturbing to the patient. Essentially the procedure consists of unilateral stimulation for 40 seconds with tap water at 7° C. above body temperature and then at 7° C. below body temperature carried out in the prone position with the head bent 30 degrees forward. This reverses the convection flow of fluid in the endolymphatic system, causing nystagmus to occur in opposite directions. In this test the time recorded is that elapsing from the beginning of irrigation until the cessation of nystagmus. The relative mildness of the stimulus enables one to carry out frequent and repeated stimulation and thus gives a more reliable index of sensitivity. Although this test may appear complicated, in actual practice it can be quickly executed.

A comparison of the results obtained has been claimed to be helpful in the differentiation of peripheral and central lesions. Thus, for example, an end-organ paresis is indicated by a decreased response on the side of the lesion regardless of the temperature used. Conversely, an irritant peripheral lesion produces an increased response on the side being tested. Even a bilateral lesion, whether irritant or degenerative, becomes apparent when this method is used. When nystagmus is induced more readily in one direction, regardless of the two temperatures used, central involvement should be suspected.[2] The technique of administering this test must be carefully adhered to; for example, the height of the water reservoir must be kept two feet above the patient's head to ensure constant rate of flow.

In cases where a perforated drum is present, cold air (Dundas Grant tube) or ethyl chloride is used in place of water. As is the case with ice water, this test is less accurate.

Another test readily carried out without complicated equipment consists of rocking the patient backward from the sitting-up position to the supine position with the head hanging over the end of the examining table. This may be called the *"head movement test."* Many modifications of this test exist. Its purpose is to determine whether or not nystagmus can be so induced (always allowing 20 seconds for its commencement). In peripheral lesions the nystagmus so induced is brief in duration while in intracranial lesions it is prolonged and readily repeated.

Electrical stimulation of the vestibular branch of the eighth cranial nerve has been used in various medical centres; it is frequently called the *galvanic falling reaction.* This method simply demonstrates the integrity of the entire vestibular arc. It has proved useful in our clinic for ruling out possible central degeneration of the vestibular nuclei when other means, such as caloric or rotation tests, have failed to produce a response. This test essentially consists of applying a direct current between the manubrium sterni and the temporal bone. The magnitude of the current required to produce a falling reaction indicates the integrity of the eighth cranial nerve. This test should be carried out by a trained technician. The authors feel that electrical stimulation of the labyrinth associated with electronic recording of the patient's responses may yield valuable diagnostic data.

At the present time evaluation of all known tests together with the development of new ones is under way.* These tests include the tilt test of Tait and McNally, the rotation test of Barany, etc., the rotating drum to study extraocular muscle co-ordination, television recording of nystagmus and so on.

CASE HISTORIES

Case 1

Mr. W., age 30, was referred by his physician in regard to the possibility of helping the hearing or prescribing a hearing aid. The patient stated that he had had meningitis in 1940; following this a gradual change in the hearing occurred until at this time he was unable to hear conversational voice. He stated that he could feel vibration, but at his occupation as a diesel engineer he could not hear spoken words. As a child he had had mastoiditis but no change in the hearing occurred following this incident. There was no other pertinent past history. Following the meningitis attack, dizziness was present for 12 months. The examination of the ear, nose and throat was negative. An audiogram showed a complete loss of hearing in both ears and conversation at 80 db. was unintelligible. Examination showed ataxia on walking with the eyes closed, with falling first to one side and then the other. Vestibular tests revealed a completely inactive vestibular nerve response. That this involved the whole vestibular arc was evident from the fact that peripheral stimulation by caloric and turning tests produced no response. We may consider that degeneration of the central nuclei had occurred, as suggested by the fact that it was impossible to elicit a falling reaction by the electrical tests. Our investigation showed that there were no functioning components of the vestibular and cochlear divisions of the eighth cranial nerve. The damage to the central nuclei of the cochlear division probably accounted for his persisting tinnitus. The patient was given lip-reading training.

*Through the generosity of the Atkinson Charitable Foundation.

Case 2

Mrs. S., age 37, was referred for vestibular examination because of recurring attacks of dizziness over the past four years, associated with a loss of hearing in the left ear and buzzing on this side of the head. An old ear infection in childhood had recurred about a year ago, and this was treated with penicillin. She had undergone appendectomy at the age of 15, and hysterectomy six years ago. The recent attacks of dizziness appeared to be rotational in type. She described six attacks in the past four years accompanied by nausea. A general physical examination by her physician, together with blood examination, did not reveal any marked abnormality.

Examination of the ear, nose and throat and sinuses was negative. The audiogram showed a 60 db. loss in the left ear, perceptive in type. Vestibular tests revealed a hypoactive response on the left side. The electrical falling test was normal. Radiographs of the internal auditory meatus and mastoids were normal. A neurological consultation was negative. A diagnosis of Ménière's disease was made, and the patient was placed on nicotinic acid therapy.

A follow-up examination is essential to rule out a cerebellopontine angle tumour.

SUMMARY

For the accurate diagnosis of a vestibular lesion, the patient must complain of displacement of surrounding objects, which may be either in the nature of a tilting or a rotational sensation. The attacks are sudden and frequently violent. There may be little evidence on physical examination to substantiate the above statement of the patient. Since labyrinthine disease usually involves the cochlea, tinnitus and deafness are nearly always present to a greater or lesser degree.

Although it is realized that there is need for improvement in vestibular testing techniques, two of the most useful and simple tests consist of stimulation of the labyrinth (1) by hot or cold water, and (2) by sudden head movements in an attempt to produce the sensation of vertigo. The patient should always be asked whether his subjective sensations resemble those artificially produced by caloric or head movement tests.

In conclusion, all existing vestibular tests have certain limitations and each examiner must establish his own norm through experience.

This work is being carried out under the supervision of Dr. J. A. Sullivan, director of the Hard of Hearing and Vestibular Clinics at St. Michael's Hospital, Toronto.

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THE ANÆMIAS*

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CLINICAL MEDICINE is developing rapidly towards precision and certainty but much of it is still frankly empirical. As a consequence, two general attitudes to the problem of anæmias are reflected in practice today. The first, and simpler, is to prescribe one of the many widely advertised hæmatinic mixtures and hope for the best. It is true that few would openly advocate such an approach. Nonetheless, too many do attempt to treat anæmia in this way. The other attitude is based on understanding. It is this approach we propose to consider briefly.

From the standpoint of clinical medicine, the anæmias should be considered as symptoms rather than as disease entities. It is certainly important to recognize and demonstrate the presence of anæmia and to determine its general type. But this is not enough. One must always ask and attempt to answer the question: why did the patient develop anæmia? Successful treatment depends as much on the answer to this question as on accurate diagnosis and classification of the anæmia itself.

Custom and habit have led most of us to rely on measurements of the red cell count, hæmoglobin level and hæmatocrit to demonstrate the presence of anæmia and to determine its type. We are prone to forget the errors to which these familiar tests are liable. Too often, we accept the results at face value. This may lead to erroneous conclusions regarding the degree and type of anæmia, failure to understand its cause, and even to a diagnosis of anæmia when none is present. With these sobering facts in mind, little more need be said here concerning the recognition and differentiation of the types of anæmia. The wise physician will not look for short-cuts to diagnosis. A careful history and physical examination are still of prime importance. Critical

*From the McGill University Clinic of the Montreal General Hospital. Presented at the Annual Meeting of the Canadian Medical Association, Vancouver, June 18, 1954.

assessment of the history and physical findings, aided by examination of the blood and illumined by an understanding of the significance of anæmia, will lead surely to accurate diagnosis and successful management in most cases.

SIGNIFICANCE OF ANÆMIA

The mass of circulating red cells represents a balance between their production and destruction or loss. It is clear that anæmia must develop when production of red cells is poor in quantity or quality and when blood loss or blood destruction outstrips the production of new cells. It follows that the anæmias may be placed in four broad groups, three of which indicate the mechanisms by which they are produced: (1) anæmia due to blood loss; (2) anæmia due to faulty blood production; (3) anæmia due to excessive blood destruction; and (4) anæmias of unknown cause.

Let us now examine these four groups in more detail.

ANÆMIA DUE TO BLOOD LOSS

Hæmorrhage is probably the commonest cause of anæmia. It may be acute or chronic. Chronic bleeding is often occult. It should always be suspected when iron deficiency anæmia is discovered. Successful treatment depends on controlling the bleeding as well as on use of iron.

ANÆMIA DUE TO FAULTY BLOOD PRODUCTION

The known dietary factors concerned in the formation of red cells may be divided into three groups: minerals, vitamins, and amino acids.

Minerals.—Iron is an essential constituent of hæmoglobin. Deficiency of iron leads to inadequate hæmoglobin production, and anæmia results. There is experimental evidence which suggests that copper, molybdenum and cobalt are also concerned in erythropoiesis. This has little bearing on clinical practice. The minute requirements of these metals are supplied adequately by even the most restricted diets. Copper deficiency may conceivably be concerned in the nutritional anæmias of infancy. But from the standpoint of practical therapeutics, these three metals can be disregarded.

Normal individuals require very little iron, and an average Canadian diet will provide enough to maintain them in iron balance. This mineral is carefully conserved by the body, only minute quantities being excreted. Iron balance seems to be maintained by regulation of absorption according to body needs rather than by excretion of unwanted excess. Thus, in normal individuals the uptake of iron is small, while in persons with iron deficiency the uptake is increased as much as tenfold. In men, iron deficiency is due almost always to blood loss, or a long-standing defect in intestinal absorption. Iron deficiency is much more common in women. This increased incidence is related to excessive menstrual blood loss, the extra demands for iron during pregnancy and lactation, and loss of blood at parturition. Increased requirements for growth occasionally lead to iron deficiency in childhood. The physician called on to treat this disorder looks first for the primary cause. He always suspects chronic bleeding even though the patient is not aware of the bleeding. Most cases respond promptly to adequate amounts of iron by mouth. Ferrous sulphate, in doses of three to five grains three times a day, is usually effective. Many other iron preparations containing equivalent amounts of elemental iron are also satisfactory. Effective preparations for intravenous use have been developed recently. These are not without some danger and should be used only in cases which cannot be treated adequately with iron by mouth.

Vitamins.—Dietary experiments with animals indicate that deficiencies of many vitamins will interfere with erythropoiesis and lead to the development of anæmia. It does not follow that all these agents need be administered to patients with anæmia. Indeed it is doubtful whether anæmia ever develops in man from deficiencies of most of these individual vitamins.

A characteristic megalocytic anæmia is encountered in pernicious anæmia. A similar and often indistinguishable blood picture is sometimes seen in sprue, nutritional deficiency and pregnancy. It occasionally results from fish tapeworm infestation and may follow gastrectomy or strictures and anastomoses of the small intestine. The response of patients with this type of anæmia to vitamin B_{12} or folic acid leaves no doubt that deficiencies of these two vitamins are important in man. The role these two substances play in the metabolic processes leading to normal blood production is obscure. However, clinical experience has demonstrated that the megalocytic anæmias can be arranged in a

spectrum according to their responses to these two agents. Pernicious anæmia has a place at one end and pernicious anæmia of pregnancy at the other. Vitamin B_{12} seems to be a specific remedy for pernicious anæmia and is replacing liver extract in the treatment of this disease. In addition to relieving the anæmia, this vitamin arrests and prevents subacute combined degeneration of the spinal cord. Folic acid is contraindicated in the treatment of pernicious anæmia because it fails to relieve or prevent this neurological complication and may even precipitate it. In pernicious anæmia of pregnancy, on the other hand, folic acid evokes a prompt response and is the agent of choice, for vitamin B_{12} and liver extract are usually not effective. The remaining megalocytic anæmias occupy intermediate positions between these two extremes. They usually respond to either vitamin B_{12} or folic acid, but sometimes to only one of them. Occasionally they fail to respond unless both agents are administered simultaneously.

Amino acids.—There are four globin molecules in one molecule of hæmoglobin. Each globin molecule contains all the essential amino acids and some of the non-essential ones. When the size and complexity of these globin molecules are considered, it is not surprising that protein deficiency can lead to anæmia. In these circumstances, no single amino acid deficiency can be shown to be responsible for the anæmia. Consequently the administration of single amino acids to patients with anæmia has little to recommend it, while attention to the provision of protein in the diet is clearly important.

ANÆMIA DUE TO INCREASED BLOOD DESTRUCTION

Normally the red cell mass is replaced about every four months. When red cells are destroyed at a faster rate, the body attempts to compensate by increased blood production. When destruction exceeds production, hæmolytic anæmia results. There are many different and quite unrelated causes of hæmolytic anæmia. A defect in the red cell itself may be responsible. Congenital hæmolytic anæmia, sickle cell anæmia and Mediterranean anæmia are examples of this. A wide variety of infections and chemical and physical agents as well as animal and vegetable poisons can produce severe hæmolysis. Malaria, sulphonamide drugs, thermal burns, fava beans and snake venoms are selected examples. Immune body reactions can be demonstrated in most cases of acquired hæmolytic anæmia. Finally, hæmolytic anæmia may complicate the course of other conditions such as the lymphomas and chronic liver disease. Some would also include here the anæmia associated with certain disorders of the spleen.

When a toxic agent is responsible, the patient should be removed from its influence. Specific infections should of course be treated. Blood transfusion is valuable and sometimes life-saving. Blood should be given cautiously because severe hæmolytic reactions sometimes occur even though the ordinary typing and cross-matching is accurate beyond dispute. Removal of plasma or washing of the donor red cells is sometimes necessary to obviate this difficulty. Splenectomy has been recommended for several of the hæmolytic anæmias. The problem is to decide which patients will benefit from the operation. Splenectomy is indicated in young persons with congenital hæmolytic anæmia. Here, success can be promised with confidence. In acquired hæmolytic anæmia, on the other hand, the value of the operation is debatable. In individual cases brilliant responses may be produced but the overall results are disappointing. In our experience ACTH and cortisone have been valuable in the treatment of this condition. Some patients achieve complete remissions and do not require further hormone treatment. Others relapse unless maintenance doses are supplied. It is our practice to reserve splenectomy for cases in which the response to ACTH or cortisone has not been maintained.

ANÆMIAS OF UNKNOWN CAUSE

We are left with a potpourri of anæmias of unknown cause. Aplastic anæmias and the anæmias associated with chronic infection, renal disorders and malignant diseases belong here. They are improved little, if at all, by treatment with minerals or vitamins. Blood transfusion is sometimes useful but is only a temporary expedient. Successful management depends on control of the underlying disorder.

CONCLUSION

We have tried to show that the intelligent management of anæmia depends on accurate

Canad. M. A. J.
Mar. 15, 1955, vol. 72

diagnosis and classification together with an understanding of its significance. Sound clinical judgment and common sense are required, for anæmia is a symptom of disease, not a disease itself.

RÉSUMÉ

L'anémie est souvent un symptôme plus qu'une maladie en soi. On ne doit pas oublier que la formule rouge, l'hémoglobine et l'hématocrite peuvent conduire à de fausses conclusions. Les anémies peuvent être divisées en quatre groupes: (1) l'anémie causée par hémorragie; (2) l'anémie causée par insuffisance de la production des globules rouges; (3) l'anémie causée par destruction accélérée des globules; (4) les anémies d'origine inconnue.

1. L'hémorragie demeure probablement la cause la plus commune de l'anémie. Elle peut être aiguë ou chronique; cette dernière souvent insoupçonnée. On doit y penser en constatant une déficience du fer. Le traitement consiste à arrêter l'hémorragie et à favoriser l'absorption.

2. Les facteurs nutritifs de la production des globules rouges peuvent être rangés en trois groupes: les minéraux, les vitamines et les acides aminés.

Les minéraux. Le fer est une partie essentielle de l'hémoglobine. L'insuffisance en fer conduit à l'anémie. L'individu en santé n'a besoin que d'une très petite quantité de fer; il assimile le fer selon ses besoins, tandis qu'un anémique en absorbera peut-être jusqu'à dix fois autant. Les femmes surtout sont sujettes à manquer de fer soit par ménorragie, soit par un plus grand besoin de fer pendant la grossesse et la lactation, soit par hémorragie à l'accouchement. La croissance peut causer de l'anémie chez les enfants. Dans tous les cas, le traitement consiste à absorber par la bouche quelques préparations de fer, par exemple: 0.15 à 0.30 gramme de sulfate de fer trois fois par jour.

Les vitamines. Une déficience en certaines vitamines peut déranger la production des globules rouges et conduire à l'anémie. On observe une anémie mégalocytique dans l'anémie pernicieuse, ainsi que dans les cas d'insuffisance nutritive et de grossesse. Elle peut aussi être causée par le ver solitaire du poisson, ou suivre une gastrectomie ou un rétrécissement ou une anastomose du grêle. La vitamine B_{12} semble le remède spécifique pour l'anémie pernicieuse mégalocytique; l'acide folique est contre-indiqué. Dans l'anémie pernicieuse de la grossesse, par contre, l'acide folique agit là où la vitamine B_{12} et l'extrait de foie restent sans résultat. Les autres anémies mégalocytiques sont traitées par la vitamine B_{12} ou l'acide folique, et quelquefois par les deux en même temps.

Les acides aminés. Par l'examen d'une molécule d'hémoglobine, on se rend compte aisément qu'une déficience en protéine peut causer de l'anémie. Au lieu d'administrer un acide aminé isolé, il vaut beaucoup mieux surveiller la richesse en protéines du régime alimentaire.

3. L'anémie hémolytique peut résulter d'une maladie des globules rouges, ou de diverses infections, ou de divers poisons d'origine animale ou végétale. Ce genre d'anémie peut aggraver certaines maladies du foie ou du système lymphatique. Les transfusions nécessitent des précautions spéciales parce que de graves réactions hémolytiques peuvent se produire. L'ablation de la rate est conseillée chez les jeunes souffrant d'anémie hémolytique congénitale. Dans les cas d'anémie hémolytique acquise, on conseille l'emploi de l'ACTH et de la cortisone, réservant l'opération pour les malades dont l'anémie persiste après essai du traitement.

4. Beaucoup d'anémies semblent d'origine inconnue et sont peu ou pas améliorées par les minéraux, les vitamines ou la transfusion. Il faut tâcher de découvrir et de soigner la maladie qui peut en être la cause.

M.R.D.

JEJUNAL SENSITIVITY*

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"Every time I eat, an express train starts up in my insides."—A patient, after gastric resection.

THE HUMAN JEJUNUM was not designed to receive undigested food, and when called upon to do so it is not surprising that it sometimes reacts quite violently. Such a situation may arise after gastric resection, especially when the stump is small and the stoma large; the impression given on fluoroscopy of many of these cases is that of a tube and funnel, the barium falling rapidly out of the stump and into the coils of the small intestine.

Jejunal sensitivity was reported long ago, many years before the operation of partial gastrectomy became fashionable, or before anybody had heard of the expression "dumping syndrome." In those far-off days there was a period when some physicians attempted to treat duodenal ulcer by means of peroral jejunal feedings administered by tube and syringe, the general idea being to avoid the passage of food over the ulcerated area. It was noticed that some patients so treated complained of nausea, of sweating, and of upper abdominal fulness, if the nutriment used was above or below the temperature of the body, or was put in too quickly.[1]

It is easy to demonstrate this characteristic of the upper small intestine in patients after gastrectomy by giving a barium meal mixed with a 50% dextrose solution. The marked spasm which may follow has been shown by Glazebrook and Welbourn,[3] the jejunum sometimes

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appearing as though it were trying to tie itself into knots.

Two groups of symptoms accompany this muscular show of jejunal resentment—local and general. The local ones are usually described as a sensation of abdominal discomfort, distension, or "wind", sometimes with nausea, aerophagy and belching; occasionally they are more intense and actual pain may be complained of; the pain is burning in character, and when it occurs many will say that it exactly resembles the pain of their former duodenal ulcer. The nausea, aerophagy and belching accompanying this pain may be superseded by actual vomiting, an act which will immediately relieve the distress, just as vomiting may relieve peptic ulcer distress.

There are also general symptoms and signs, and their number, duration, and prominence increase with the violence of the local sensations. They may be absent, or be represented by nothing more than a dampness of the forehead and palms. In others, the production of palpitation, pallor, weakness of the legs, and hypotension leads to an urgent desire to lie down, and especially sensitive patients may faint. This collapse may last for 15 to 20 minutes, and in one case was so profound I feared the patient had died. Rarely the outstanding outward sign of the jejunal hypermotility may be sweating so copious that it literally pours off in streams, a dramatic and unusual reaction difficult to visualize until it has been seen. These phenomena do not occur in all, and many patients can take the dextrose-barium mixture with impunity.

The resemblance of the local discomfort or pain to duodenal ulcer discomfort or pain is all the more striking because it is usually referred to the middle line between the umbilicus and the xiphisternum, and tenderness during the examination can be elicited here, although it is some way from the jejunum. It is important to realize that tenderness over this point is not due to duodenal inflammation or ulcer in these patients, and perhaps even in people with intact stomachs this sign is not a reliable indication of duodenal involvement.

Tenderness can also be found directly over the spastic loops of small bowel in the left lower quadrant, and in thin patients it may be possible actually to palpate the knotted loops as firm oval masses, the size of a Victoria plum, which disappear when the spasms pass away.

Within 20 minutes, the bowel spasms commence to relax and in a few a burst of peristaltic activity will follow so that within half an hour of taking the barium most of it will be passed as a semi-fluid stool. In others a prolonged period of atonicity and hypomotility may show as an obstinate constipation, which I have known to last for as long as 12 days. In either case, with the easing of the jejunal cramps the symptoms both local and vasomotor pass, leaving, if they have been severe, a weakened patient whose one desire is to sleep.

KYMOGRAPHIC INVESTIGATION

In people with intact stomachs, it is not possible to demonstrate jejunal sensitivity by means of a dextrose-barium meal, the delay in passage through the stomach being quite sufficient to abolish the irritant action of this mixture, and another method must be used.

A Miller-Abbott tube with attached balloon is allowed to pass through the duodenum into the jejunum, its position being checked by x-rays. If it will not pass easily and quickly, I allow the balloon to lie in the pyloric canal overnight, giving the patient a soft evening meal, and a barbiturate for sleep; it is usually in the desired place by next morning in a patient undisturbed by over-handling.

The balloon is slowly inflated with 20 c.c. of air and connected to a recording kymograph. Test solutions may be injected directly into the jejunum, through the suction lumen of the tube, the disturbing effects of hot or cold solutions, of sudden overdistension by syringe pressure; or of irritant fluids such as hypertonic sugar solutions or concentrated protein emulsions, may easily be seen. Although the rubber balloon is an unusual bolus for the jejunum to swallow, it is not common for it to arouse marked peristalsis; and water, normal saline, and isotonic sugar solutions also fail to cause upset, provided that they are warmed to body temperature.

Fig. 1 sets out diagrammatically the effects of the intra-jejunal instillation of 30 c.c. of a 50% dextrose solution in a normal subject. On the left the normal jejunal contractions are recorded; in the centre, waves of the enhanced amplitude which follow the contact of the hypertonic solution with the bowel wall are seen; and to the right the diminished contractions and the tonal loss, which may follow spontaneously, or be

Canad. M. A. J.
Mar. 15, 1955, vol. 72

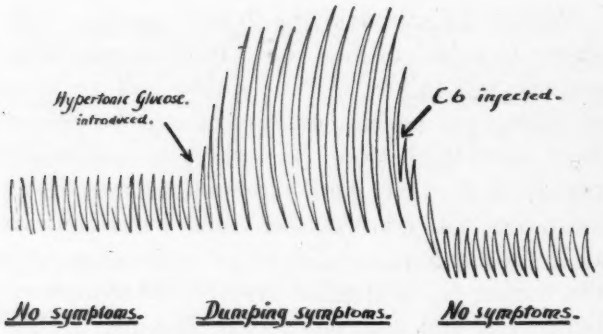

Fig. 1.—Diagram illustrating the kymographic investigation of the dumping syndrome.

produced by the injection of 50 mgm. hexamethonium bromide (C 6), appear, and the diminished tonus is indicated by a fall in the baseline as compared with the original writing. The "dumping symptoms" so produced vary from one patient to another, their onset and duration corresponding to the increased intestinal muscular activity. They are not caused by gravity pull as claimed by Capper,[2] because the experiment works equally well whether the subject is erect or prone. The symptoms, besides being diminished by C 6, may also be ameliorated by the further slow introduction into the jejunum of 100 c.c. of warm water, which dilutes the irritant sugar. This fact does not support Machella's theory,[4] which attempts to implicate gut distension by osmotic pressure as a cause of the discomforts, although, as has already been mentioned, sudden forcible distension by syringe pressure will produce them.

JEJUNAL SENSITIVITY

Ten per cent of the men and 20% of the women investigated by us were found to have jejunal sensitivity. These percentages are taken from a group of over 1,000 patients but it must be stressed that they do not represent a fair sample of the population, as all of this work was done upon people admitted to hospital with gastro-intestinal complaints.

The condition of "jejunal sensitivity" was judged to be present when the introduction of 30 c.c. of a 50% dextrose solution into the jejunum produced such an excessive response, with severe symptoms and extreme kymographic excursions, that the recording had to be stopped. In addition, evidence of jejunal intolerance to solutions usually innocuous was given in this group, and in some the balloon itself was not received without protest.

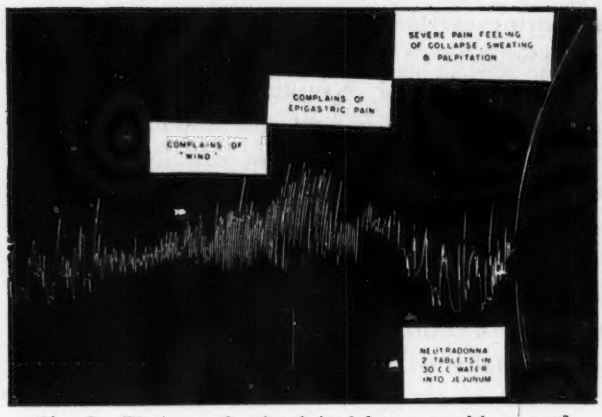

Fig. 2.—Photograph of original kymographic record.

Fig. 2 exhibits such a reaction. It is an actual recording from a patient, in whom there was a steady increase in jejunal activity, presumably due to the presence of the balloon; as this activity increased, the early complaint of "wind" was succeeded by epigastric pain. This died away, perhaps as the gut became accustomed to the balloon, but the instillation of a belladonna preparation, which is normally followed by hypoactivity as the belladonna becomes absorbed, produced an immediate violent increase in motor movements. The symptoms which appeared as concomitants were so acute that the air had to be released from the balloon and the recording stopped. The effect of introducing a cup of hot sweet tea into such a jejunum may be well imagined.

Sensitivity is not related to the pattern of jejunal motility before stimulation; it may be found in a gut which appears quite inactive, whereas a small bowel showing a great excess of motor activity will not necessarily respond in a dramatic way to strong solutions or to hot or cold substances.

ACTION OF ANTICHOLINERGICS

It might be thought that the anticholinergics, with their strong depressant action on small bowel movements, would prevent the jejunal response described above. This is not the case, even when they are used in full therapeutic dosage.

Fig. 3 shows on the left the paralysis of jejunal activity which has been produced by the subcutaneous injection of 1/100 gr. (0.65 mgm.) atropine. In spite of this, brisk and immediate contractions of the bowel with symptoms were set off by the introduction of 30 c.c. of 50% dextrose solution.

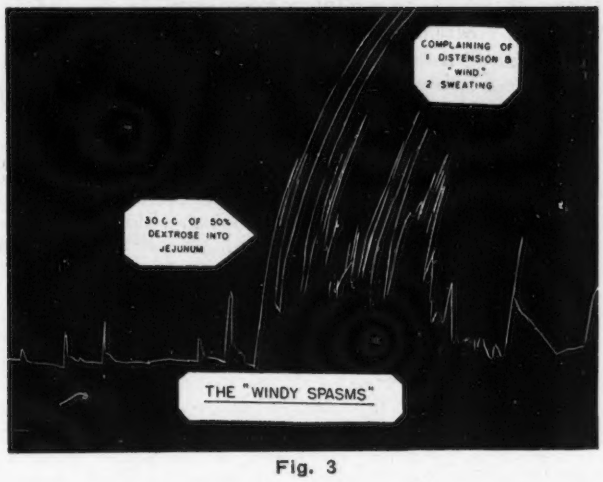

Fig. 3

The same sort of thing occurs if any of the newer anticholinergics are used, although they may curb the more violent excursions. This explains their frequent failure to control post-gastrectomy symptoms.

Compounds which block the action of barium chloride upon smooth muscle, rather than the action of acetylcholine, such as WIN 1723, WIN 5786,[5] and chlorpromazine, are more successful in inhibiting locally produced spasm, but unfortunately their side-effects may not be helpful to the patient.

Clinical Applications

I do not know what part jejunal sensitivity may play in the symptomatology of gastro-intestinal disease before operation, but the signs and symptoms it produces resemble those seen in the post-gastrectomy dumping syndrome and it is difficult to avoid the conclusion that it must be one of the factors involved in the production of sequelæ after gastric operations, although it should not be regarded as the only one.

Its presence should be suspected in cases of duodenal ulcer where the complaint of pain and discomfort before operation seems out of proportion to the demonstrable lesion. When there is hesitancy in advising operation, because of lack of definite surgical indication, such as hæmorrhage, perforation, obstruction or malignancy, a kymographic investigation is worth ordering.

The presence of jejunal sensitivity is an indication for persevering with medical treatment. If operation must be performed, gastro-enterostomy should be considered in cases with low gastric acidity, as severe postoperative symptoms are liable to follow gastric resection, and they may turn out to be even more intractable and incapacitating than the original ulcer.

A high acid curve rules out simple gastro-enterostomy, because of the danger of stomal ulcer; and then every effort should be made to perform the Billroth I type of resection, which makes an attempt at restoration of anatomical continuity, rather than the Billroth II.

Unfortunately, it may be found at laparotomy that the Billroth I is not a practicable proposition, and that the Billroth II is the only feasible procedure. Then I feel the surgeon is in a quandary. If he removes too much stomach, the post-gastrectomy syndrome will be severe; if he removes too little, a stomal ulcer is likely to occur. Too large a stoma, which allows food to be dumped precipitately into the jejunum, is not helpful either; but again I believe that too small a stoma also encourages inflammation and ulceration. It would seem possible that knowledge of jejunal sensitivity, such as could be provided by preoperative motility studies, would assist the surgeon in choosing the best method in individual cases.

Summary

The phenomenon of jejunal sensitivity has been described and its clinical applications have been discussed.

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SAFETY OF SPINAL ANÆSTHESIA

The most vociferous objection to spinal anæsthesia comes from those who believe that chronic, incapacitating neurological disease occurs with sufficient frequency after spinal anæsthesia to make its use unjustified except in rare instances. It is not scientific thinking always to attribute to the anæsthetic a neurological complaint arising in a patient who has had spinal anæsthesia. Other diagnostic possibilities must be kept in mind constantly lest specific therapy be withheld because of an error in diagnosis. Physicians appear prone to assume a cause and effect relationship between spinal anæsthesia and a variety of complaints, sometimes appearing years after the anæsthesia. This attitude is not objective, nor is it justified on the basis of available data.—*J. A. M. A.*, **156**: 1491, 1954.

Canad. M. A. J.
Mar. 15, 1955, vol. 72

Case Reports

PULMONARY COMPLICATIONS DURING TREATMENT WITH HEXAMETHONIUM*

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A FEW CASES of interstitial pulmonary infiltration have been recently reported in hypertensive patients treated with hexamethonium salts alone[1] or in conjunction with hydrazinophthalazine.[2] The case to be reported is an instance of such a lesion developing in a patient who received hexamethonium chloride for a period of over six months.

The patient, a 28-year-old woman, was admitted to the Hôtel-Dieu Hospital in June 1953, complaining of shortness of breath, headaches, dizziness, back pain, nausea and vomiting.

When first seen here in 1947 at the age of 22, she had complained of dyspnœa, was pale and had a generalized œdema of recent onset, preceded by recurrent upper respiratory infections of two years' duration. Her blood pressure was then slightly elevated, ranging from 140 to 170 systolic and 90 to 110 diastolic. The serum protein level was 3.5 gm. per litre, with 1.5 gm. of albumin. There was a proteinuria of 12 gm. per 24 hours, with microscopical findings of red cells, hyaline and granular casts, and numerous birefringent bodies. The basal metabolic rate was minus 21. From 1947 to 1953, the clinical course of this mixed-type glomerulonephritis was characterized by exacerbations and partial remissions of a predominating nephrotic syndrome, with a late evolution towards the terminal stage as indicated by progressive nitrogen retention, deterioration in renal function, disappearance of œdema and sustained hypertension.

On admission, the patient showed evidence of a marked loss of weight and appeared chronically ill. On physical examination, her blood pressure was 186/144, and a gallop rhythm with a snapping aortic second sound was heard on auscultation of the heart. Examination of the fundi revealed bilateral papillœdema and marked vasoconstriction of the arterioles with scattered hæmorrhages and exudates. There was no sign of peripheral œdema. Renal function was markedly impaired, as shown by a blood urea of 0.9 gm. per litre, a urea clearance at 8% of normal, a urinary excretion of phenolsulphonphthalein at 11% after 70 minutes, and a retarded excretion of Diodrast. Urinary specific gravity was fixed at 1.006. Total serum proteins, albumin and cholesterol were normal. Chest radiography revealed enlargement of the left heart, but the lung fields were clear. The electrocardiogram was interpreted as showing left ventricular hypertrophy and strain.

The rapid deterioration in the patient's general condition, the persistence of the papillœdema and the steady rise in blood pressure to diastolic levels of between 140 and 170 mm. were considered as evidence of a malignant form of hypertension superimposed on chronic glomerulonephritis. A diet containing 35 gm. of protein with less than one gram of sodium chloride was prescribed, and 25 mgm. hexamethonium chloride was injected subcutaneously at twelve-hour intervals. Under this regimen, the blood pressure came down rapidly to normotensive levels and, save for a few bouts of diarrhœa, the side-effects of the drug were minimal. The patient was discharged on September 9, 1953, free of headaches and nausea, but still showing the same degree of papillœdema as on admission.

After discharge, the patient was observed at weekly intervals in the hypertension clinic. As outlined in Fig. 1, the blood pressure, especially in the supine position, rapidly returned to markedly hypertensive levels despite a progressive increment in the dosage of hexamethonium, and she was readmitted on November 20, because of severe headaches, marked asthenia and nausea. On physical examination, she did not show a marked change from her previous state. There was slight papillœdema and a few congestive rales over both lung bases. There was no modification of the results of kidney function tests.

On December 21, the patient complained of a severe catching pain over the lower side and back of the left hemithorax. A loud friction rub was heard over the same area. On chest roentgenograms, a diffuse infiltration of both lower pulmonary fields was seen, which by January 7 had progressed to a diffuse nodular infiltration of both lungs (Fig. 2). There was a minimal, nonproductive cough with moderate dyspnœa. No cyanosis was observed and the temperature remained normal at all times.

Although the blood pressure was controlled at moderately hypertensive levels and the papillœdema had completely disappeared, the patient became cachectic and extremely asthenic, and died in uræmic coma on February 4. At the time of death, her height was 152 cm. (5 ft. 1 in.) and she weighed 70 pounds.

AUTOPSY

The description of autopsy findings will be limited to the kidneys and the lungs. The right kidney weighed 48 gm., the left 42 gm. Their surface was granular and did not show any petechiæ or hæmorrhagic spots. In histological sections, there was marked glomerular and tubular atrophy. Nowhere could any necrotizing arteriolitis be demonstrated, although the arteries showed marked thickening of the media and of the intima with duplication of the internal elastic lamina. The right pleural cavity contained about 100 ml. of amber fluid. The visceral and parietal layers were smooth, glistening and entirely free of adhesions. The left pleural cavity was completely obliterated by loose fibrous adhesions. The right lung weighed 590 gm., the left 380 gm. Both lungs were uniformly reduced in size. They were heavier than normal, of firm elastic consistency and subcrepitant on pressure. Seen through the unaltered visceral layer of the pleura, the

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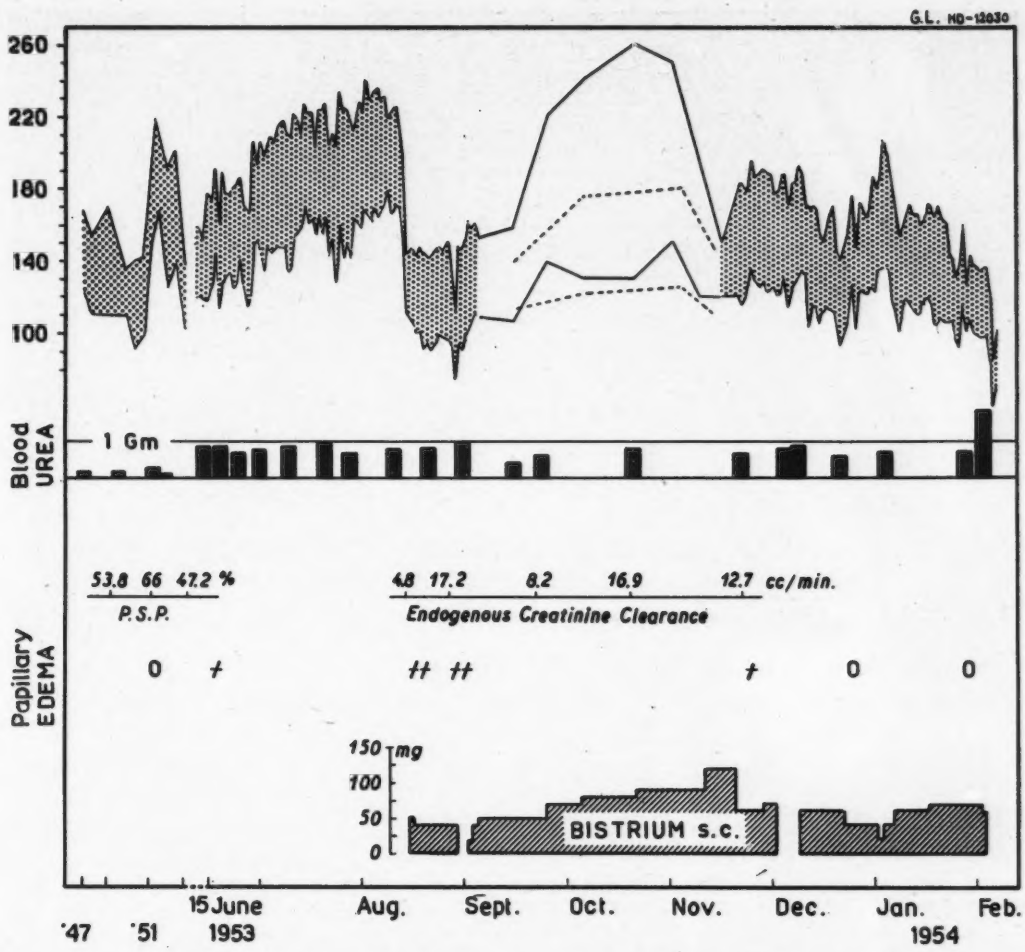

Fig. 1.—This chart summarizes the course of this case. The interesting findings are the disappearance of the bilateral papilloedema under hexamethonium therapy, the fall in the blood pressure, and the absence of any hypertensive encephalopathy. The broken lines in the upper and central part of the graph represent the blood pressure readings with the patient in the standing position, whereas the continuous lines represent blood pressure readings with the patient recumbent.

lung parenchyma was bright red, except at the apex where patches of anthracosis were seen. The surface section was smooth, moist, and bright red, and under compression released a moderate amount of serous fluid. The changes were most prominent in the lower lobe, where the parenchyma showed a gross appearance suggestive of early carnification. The left lung showed the same findings except at the apex, where the structure was suggestive of bullous and alveolar emphysema. The smaller bronchi contained a small amount of serous turbid fluid. In the larger bronchi, only a scanty amount of frothy fluid was seen.

In all histological sections, microscopical examination revealed changes qualitatively identical but quantitatively different. At low magnification (Fig. 3) the bronchial lumina appeared patent, empty, and slightly dilated, so that, in transverse sections, their cavity was circular and their wall relatively thin. Everywhere, the lung parenchyma had the appearance of coarse spongy tissue. The alveolar walls were diffusely thickened. The air spaces were only partly expanded, although not slit-like. Except for the presence of occasional air bubbles in the alveolar sacs, they were half filled with a faintly coloured fluid.

At higher magnification (Fig. 4), the thickening of the alveolar walls was seen to be due not so much to dilatation of capillaries as to the presence of a clear interstitial fluid and of numerous very fine reticulin and collagen fibrils. There was no change in the structure or the elastic fibrils. Here and there, there was interstitial infiltration of round cells, which collected in denser aggregates in the adventitia of the respiratory bronchioles and smaller pulmonary vessels (Fig. 5). Around the larger vessels and bronchi, the connective tissue was devoid of round cell infiltration. The inflammatory cells were in major part lymphocytes, admixed with a small number

Canad. M. A. J.
Mar. 15, 1955, vol. 72

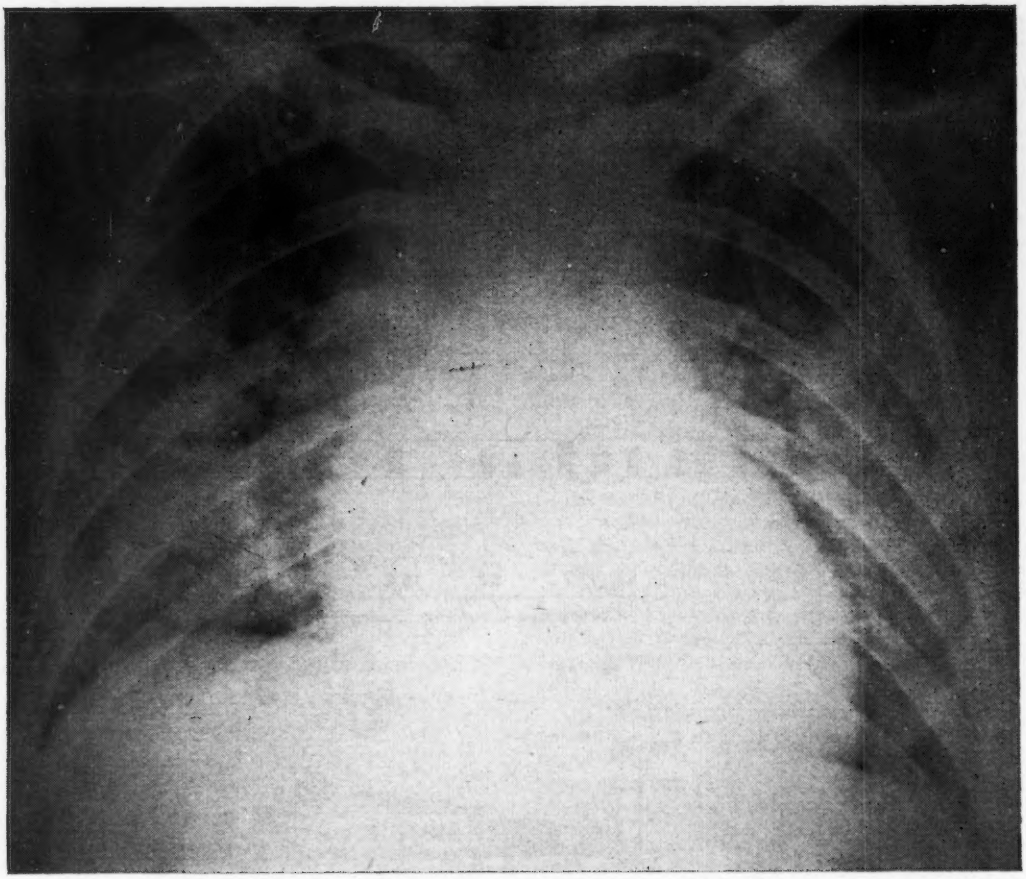

Fig. 2.—Roentgenogram of the chest taken on December 1, 1953, showing an enlarged heart and a nodular infiltration of both lower lung fields.

of plasma cells, histiocytes and polymorphonuclear leucocytes. The air spaces were lined with a nearly continuous lining of acidophilic flattened alveolar cells which tended to exfoliate in the alveoli. In a few places, the cells were multinucleated and reminiscent of the plasmodes of giant cell pneumonia, but were devoid of intranuclear and intracytoplasmic inclusions. Nowhere were hyaline membranes, fibrinous plugs or intra-alveolar fibrous buds to be seen. The

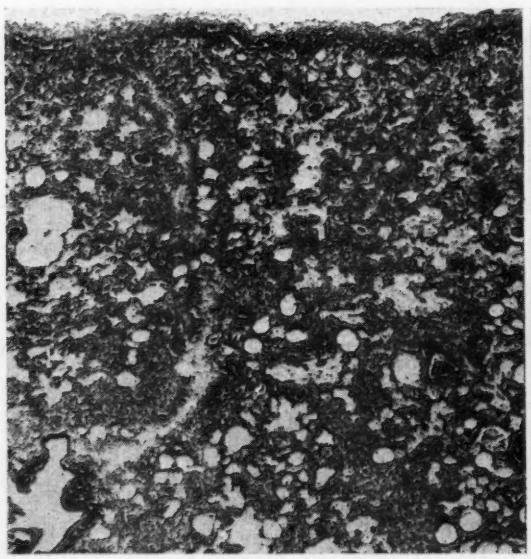

Fig. 3

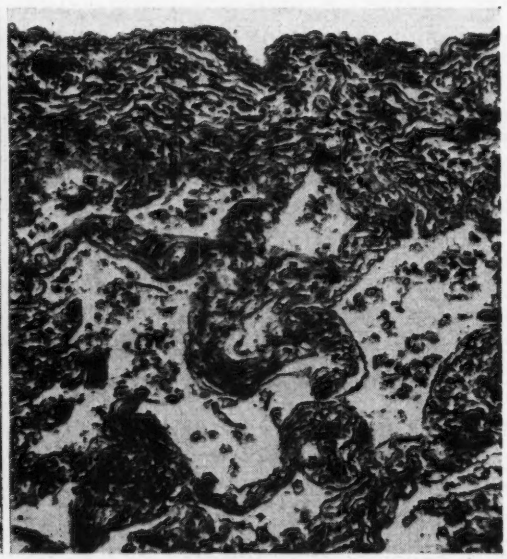

Fig. 4

Fig. 3.—x 22. Weigert elastic tissue stain; hæmalum phloxin saffron. A low-magnification photomicrograph illustrating the integrity of the visceral pleura, the diffuse thickening of the alveolar framework and the patency of air spaces. Fig. 4.—x 170, Masson's trichrome. A medium-magnification view of cortical lung parenchyma, showing fibrosis of the alveolar walls and discrete infiltration with round cells.

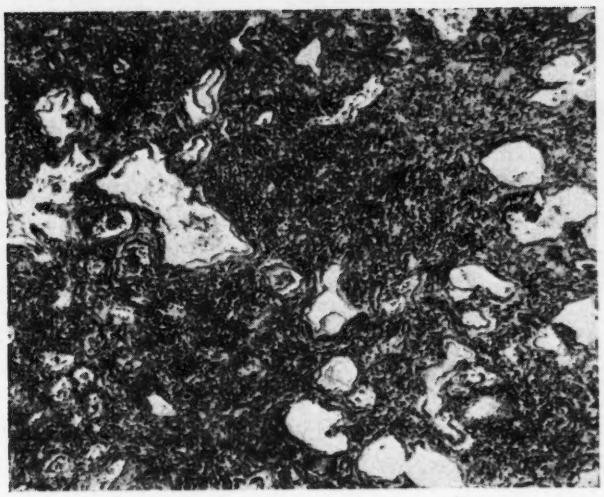

Fig. 5.—x 170, hæmalum phloxin saffron. A low-magnification view an area of more pronounced inflammatory infiltration, with collections of mononuclear cells.

alveolar exudate consisted of faintly acidophilic serous fluid and mononuclear cells. In places, a few neutrophils or erythrocytes were found. At their present stage of development, the lung changes were thus characterized less by alveolar exudation than by interstitial infiltration with mononuclear cells, accompanied by early diffuse fibrosis of the alveolar walls. The anatomical diagnosis ran thus: (1) malignant hypertension (clin.); (2) chronic arrested glomerulonephritis with pronounced atrophy of both kidneys; (3) interstitial pneumonia with early fibrosis; (4) left pleural obliteration by loose fibrous tissue; (5) left ventricular hypertrophy; (6) atheroma of the aortic valve and pronounced atheroma of the abdominal aorta; (7) passive congestion of the liver and spleen.

Discussion

As in the cases reported by Morrison[1] and by Morrow, Schroeder and Perry,[2] this patient had malignant hypertension and presented during her illness a pulmonary infiltration for which no apparent cause could be found other than the prolonged administration of hexamethonium.

Morrison describes the pulmonary lesion in one of her cases as "a central induration of both lungs due to extensive carnification regarded as the result of organization of an intra-alveolar fibrinous exudate." In five cases treated by Morrow, Schroeder and Perry with a combination of hexamethonium and Apresoline, the interstitial pneumonia is reported as identical to the acute diffuse interstitial fibrosis of the lungs described by Hamman and Rich.[3] The pathological findings in the case reported here also conform to this last description.

In contrast, however, to four of Morrow's patients who died of their pulmonary lesion within a week, our patient showed moderate respiratory impairment. It is our impression that the pleural involvement directed our attention to a pulmonary complication in its incipient stage, and that the patient died of renal insufficiency before the fibrotic process of the lung had progressed far enough to cause marked respiratory impairment. The pathological description of an early stage of interstitial fibrosis in this patient's lungs would tend to support this view.

Summary

A case of interstitial pulmonary infiltration is reported, as a complication in the treatment of malignant hypertension by hexamethonium.

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BILATERAL ALVEOLAR CELL CARCINOMA

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Primary carcinoma arising multicentrically from the alveolar cells of the lung is rare. It is especially rare when it involves both lungs equally throughout. It is reported variously as alveolar cell carcinoma, alveolar cell tumour, pulmonary adenomatosis, *epithelioma alveolaire*, and *pseudo-adenomatose pulmonaire*. There are about 60 cases reported in the literature. The first case was reported by Malassez in 1876.

It is not certain whether the disease arises from ectodermal or mesenchymal tissue. It seems as though the alveolar cells alone are involved. The septal structures and bronchi remain free. The tumour, as in our case, is often made up of high, cylindrical, mucus-producing cells forming papillary projections into the alveoli. The neoplasm has a striking similarity with jaagziekte, a fatal pulmonary condition found in sheep in Iceland, Africa and Montana, U.S.A. Jaagziekte

Canad. M. A. J.
Mar. 15, 1955, vol. 72

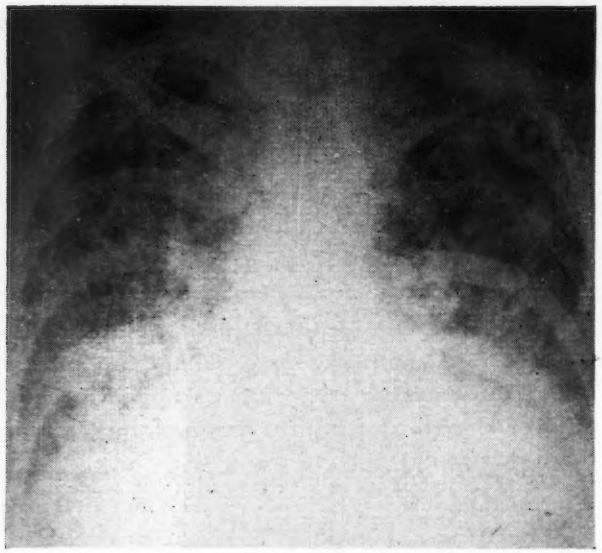


Fig. 1.—Multiple, nodular infiltration of lesion in both lungs; in places, nodules tend to become confluent.

is supposed to be due to a virus which can be transmitted from one sheep to another but not to laboratory animals. Inoculation of the tumour cells into the lungs of sheep, dogs and rhesus monkeys, and into the anterior chamber of guinea-pigs, has not resulted in reproduction of the tumour (Good *et al.*, 1950;[5] Davis and Simon, 1950).

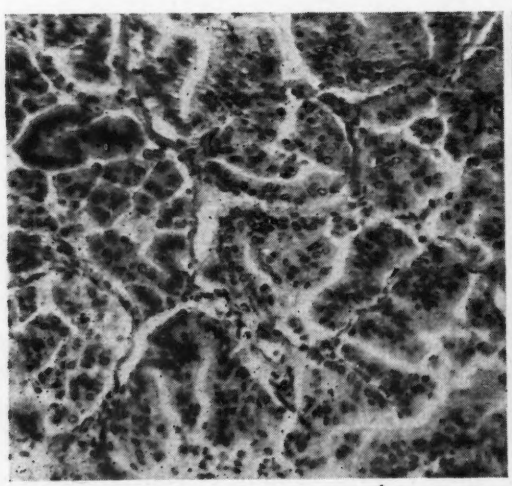
Carcinogenic agents have been hinted at as a possible cause of alveolar cell tumours, but the evidence is not conclusive. Several conditions in human subjects, in which the pulmonary alveoli become lined with epithelial cells in response to inflammation, and in which the septa are thickened, resemble this condition. But in alveolar cell tumour the septa are not thickened.

According to Swan, three criteria will have to be satisfied before the diagnosis of alveolar cell tumour is made: (1) proliferation of the alveolar cells with tall, columnar, mucus-producing cells in the alveoli; (2) no bronchial tumour; (3) no primary adenocarcinoma elsewhere in the body that could give rise to metastases into the lungs. Greever and Newbuerger in 1942 in their study of several cases concluded that alveolar cell carcinoma and pulmonary adenomatosis were indistinguishable.

There are two varieties: (1) the multiple, nodular, with miliary to marble-size nodules about evenly distributed throughout both lungs; (2) the diffuse, involving a single lobe of a lung and perhaps spreading to other lobes, pneumonic in radiological and microscopical appearances.

In a study of 51 cases carried out by Griffith *et al.*[6] of the Mayo Clinic in 1950, 41% were in males and 59% in females: 61% were in the fifth decade. The ages were from 17 to 89 years. In 69% the disease affected both lungs; 50% were of the nodular and 50% of the diffuse variety; in 48% there were metastases. The chief clinical symptoms were dyspnœa 67%, productive cough 43%, non-productive cough 35%, hæmoptysis 27%, and thoracic pain 18%. The average duration of symptoms was two months.

In our case the most marked symptom was extreme shortness of breath along with a choking sensation. This was present for two weeks. Cough, at first non-productive, was present for 10 months. The treatment in those cases that do not lend themselves to surgery is very ineffective. Radiation therapy is of little use. Radiologically the picture is often confused with bilateral generalized tuberculosis, the multiple nodular form



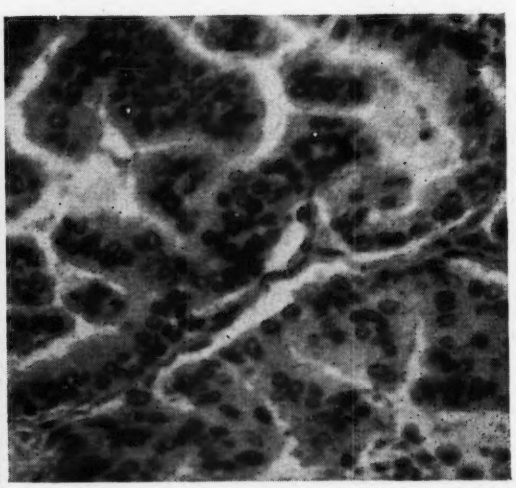


Fig. 2.—Photomicrograph of section of lung showing the alveoli filled with carcinoma cells with preservation of the alveolar septa (courtesy of Prof. Carlton Auger). x 205. Fig. 3.—Photomicrograph, high power, showing the cylindrical form and mucus-producing nature of these carcinoma cells (courtesy of Prof. Carlton Auger). x 420.

with pneumoconiosis and the diffuse form with virus pneumonia.

The diagnosis of these cases clinically is very difficult. A definite diagnosis can only be made by lung biopsy or at autopsy. Occasionally examination of the sputum may give a lead to the diagnosis. Even bronchoscopy is often not helpful.

Mrs. . ., age 60, first consulted me on December 27, 1953. Her chief symptom was marked dyspnœa. She complained of cough, non-productive at first but later productive, for the past ten months. She said she took a cold in February 1953, from which she did not recover. She had lost 31 lb. in weight over the past four months. She denied any hæmoptysis. At times, she claimed, she ran a high fever.

Her family history was irrelevant except that her mother died of cancer. There was nothing in her personal history of a carcinogenic nature. She had lived on a farm all her life but had never tended sheep.

On physical examination she was thin and weak. It was evident that she had lost weight. What stood out most markedly was her extreme dyspnœa but cyanosis was not marked. Ears, nose, throat and neck were essentially normal. There were no enlarged lymph nodes in her neck. Her heart was large; the transverse diameter was 5¾ inches, rate 110, regular, no murmurs. B.P. 180/80. Lungs were dull to percussion, expansion was poor. There was no ascites. Pelvic and rectal examinations were negative. There was no œdema of the extremities. There were no palpable lymph nodes. The temperature was 96° F., the urine was negative and the erythrocyte sedimentation rate (Westergren) was 30.

A radiograph was taken of the chest and a diagnosis of advanced bilateral pulmonary tuberculosis with moderate hypertension was made.

Subsequent examinations of the sputum by direct smear and by inoculation into a guinea-pig did not reveal the presence of tubercle bacilli.

The patient died on January 13, 1954, eight days after having been admitted to hospital and 17 days after I had first seen her. Radiographs of the chest (Fig. 1) show the multiple nodular, widespread dissemination of the lesion throughout both lungs. Figs. 2 and 3 show sections of the lungs.

The pathological findings (Dr. Carlton Auger, Professor of Pathology, Laval University, Quebec) were as follows: "Tissue sections from all pulmonary lobes were received in fixative for histological examination. All were more or less completely invaded by a carcinoma, and, except in a few sclerotic foci, with conservation of the bronchi and the general alveolar pattern. The neoplasm was made up of high columnar cells which formed an irregular epithelium lining the alveolar septa with many folds into the lumina. Most cells contained muci-carminophilic material and mitotic figures were relatively few.

"A piece of liver and of spleen was also sectioned. It showed stasis, without any metastases.

"Diagnosis: alveolar carcinoma of the lung, also called pulmonary pseudo-adenomatosis."

As noted above, there were no metastases. The lesion in the lungs was multicentric. No other primary focus was found elsewhere in the body.

I am greatly indebted to Dr. Carlton Auger, Professor of Pathology, Laval University, Quebec, for the pathological examination, for his kind report and for the photomicrographs which are here shown; to Dr. P. Duval, Medical Director, Macamic Sanatorium, and his staff for their valuable work and for supplying radiographs and photographs, and to Dr. George H. Bergeron, Youville Hospital, Noranda, P.Q., for his interest and literature.

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MULTIPLE INFESTATION WITH DIPYLIDIUM CANINUM IN AN INFANT*

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DIPYLIDIUM CANINUM is a common parasite of dogs and cats and is cosmopolitan in distribution. Venard[1] states that more than 50% of the dogs in the United States are infected with *D. caninum*. Man is rarely affected, but over 90 cases, mostly in Europeans, have been reported[2] and many may be unreported. A case in a child in Canada was recorded in 1949 by Kuitunen-Ekbaum.[3]

Most of the patients are children. In Blanchard's series,[4] 30% were under six months and 85% under eight years of age. The youngest

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Canad. M. A. J.
Mar. 15, 1955, vol. 72

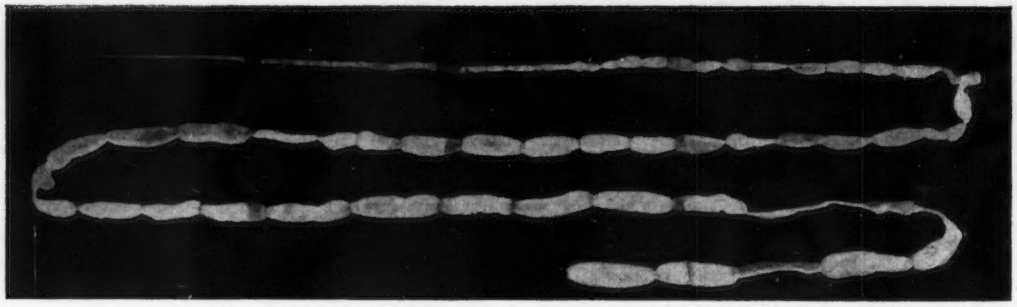

Fig. 1

child was five weeks old. Multiple infestation is rare[5] despite the fact that one flea may harbour one or a few *Dipylidium* larvæ or as many as 40 or 50.[3] Brandt (cited by Blanchard) has reported two cases of heavy infestation with 48 and 30 worms.

Segments of the tapeworm are discharged in the fæces of infected human subjects and animals. These may be slowly motile when freshly passed and may suggest pinworms to an inexperienced mother. It is unusual to find ova in the stools because the proglottides rarely expel them or disintegrate within the host. When the proglottides disintegrate, some of the liberated ova become embedded in the animal host's hair, especially the perianal hair. Here they are ingested by the intermediate host—the dog flea, cat flea, human flea, or dog louse—and in this host they develop into infective cysticercoids. Man is infested by swallowing these fleas. The greater incidence of infestation in children than in adults may result from their closer association with household pets, which often lick their faces, toys, and eating utensils.

J.C., a 13-month-old female infant, was in perfect health with normal development when seen at the Hospital for Sick Children. There was no history of gastrointestinal or other upset, and physical examination revealed a normal healthy child.

During the two weeks before admission, a few motile whitish flat segments, about ⅜ x ⅛ inch in size, were noted by the mother in almost every stool. A dog and a cat were kept in the house, but there was no illness or signs of parasitic infestation in them. The infant continued to pass the ivory-coloured segments, which were identified as mature and gravid proglottides of the dog tapeworm. Ova were not found in the stools.

Treatment consisted of a saline purge with one dram of magnesium sulphate given in the evening, followed the next morning by two doses of 0.2 gm. of extract of male fern administered through a stomach tube at one hour's interval. Three further doses of magnesium sulphate and an enema were given during the next few hours. No food except clear fluids was allowed during the course of treatment.

From the returns of the enema, six dog tapeworms were removed. Three more were passed the following

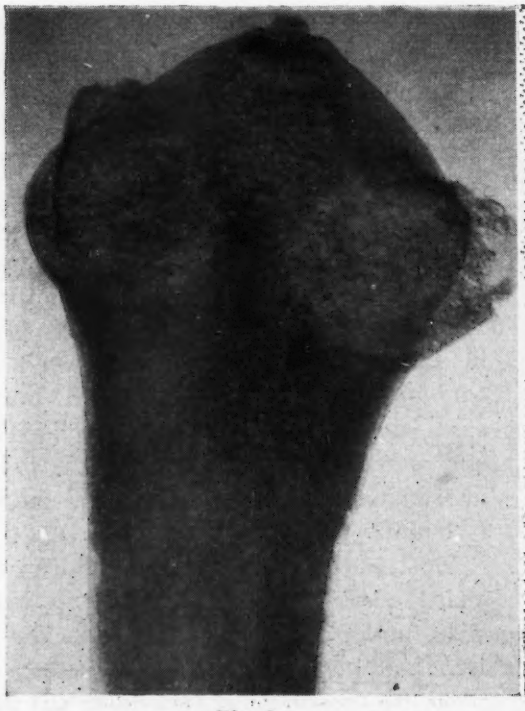

Fig. 2

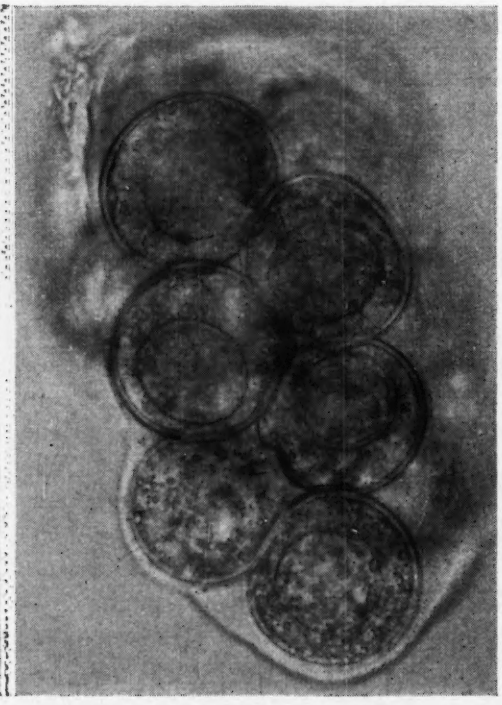

Fig. 3

day. All were complete as far as the neck, but only three were intact with heads. Their lengths varied from 8 to 20 inches. Figs. 1, 2, and 3 show respectively: a complete worm with some of the mature pumpkin-seed-like mature proglottides; an enlargement of the scolex showing two of the four suckers, the rostellum and a number of hooklets; a typical cluster of ova enclosed in an embryonic membrane. This latter was expressed from a mature proglottide. Embryos, some with indefinite hooklets, are visible within the ova.

There were no untoward effects from the treatment. The infant was readmitted to the hospital after 14 days because she continued to expel segments, though these were fewer in number and smaller than those found previously. The course of treatment was repeated and only a few short chains of immature and mature proglottides were recovered. In the following months, further segments were not found in the fæces.

COMMENT

A case of *Dipylidium caninum* infestation in an infant is described. Such a case is unusual according to our hospital records. Its infrequent occurrence is interesting in view of the high incidence of the parasite in household pets, but is understandable because of the method of acquiring the infestation—by ingestion of an infected flea.

Multiple infestation with *Dipylidium caninum* appears to be very unusual. This is more difficult to understand because an infected flea may harbour large numbers of larvæ.

The absence of symptoms, as in this case, is common in *Dipylidium caninum* infection. Often the infection is brought to notice only when segments are seen in the child's stool by the mother. In some cases of infestation, the children may experience slight intestinal discomfort, epigastric pain, anal pruritus, and reflex symptoms.

We wish to thank Dr. C. Collins-Williams for permission to report this case.

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BICARBONATE WITH SALICYLATE

The observations in the present study of children with rheumatic fever suggest that sodium bicarbonate is unnecessary in salicylate treatment. In one of the two cases of severe intolerance to the salicylate bicarbonate did not help. With sodium bicarbonate it was much more difficult to attain therapeutic serum-salicylate levels, and a much wider range of doses was necessary.—*The Lancet*, 2: 1198, 1954.

Clinical and Laboratory Notes

PROPOSAL FOR THE DISTRIBUTION OF A CERTIFIED STANDARD FOR USE IN HÆMOGLOBINOMETRY*

PREPARED BY THE DIVISION OF MEDICAL SCIENCES, NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

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THERE IS PROBABLY no procedure more commonly used in clinical laboratories than hæmoglobinometry and few that are less satisfactory in their results. The deficiencies may reside, in part, in inadequacies of the chosen method. In larger part, however, they result from manipulative errors in the measurement and processing of the samples of blood. The latter involve questions of technical proficiency which are entirely within the control of the analyst himself. When, however, he converts his observations—such as gasometric or photometric readings or measurements of specific gravity—to grams of hæmoglobin in 100 ml. of blood, he must depend upon his own calibration or a calibration supplied by an instrument maker, both procedures involving a conversion factor taken from the literature. To be satisfied that the calibration remains valid for the instrument, reagents, and technical routines in use in his laboratory, he should periodically undertake a precise and time-consuming series of standardizations. If a uniform hæmoglobin standard were available nationally and a single method of analysis widely practised, the individual laboratory would then have assurance not only that its results would be comparable from month to month, but that they would also be comparable with those from other laboratories employing the same standard. Inconsistencies in results that persisted under these conditions could then be clearly attributed to technical and manipulative errors.

The purpose of this report is to describe a plan for the distribution of a certified hæmoglobin standard and to advocate the wide adoption of a recommended analytical procedure. The use of both the new procedure and the standard is recommended. At the same time it is pointed out that the standard may be employed for the calibration of other methods of hæmoglobin analysis in laboratories that do not choose to adopt routinely the advocated photometric procedure.

In 1941 the Medical Research Council of the United Kingdom instituted an extensive study of the problem

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Canad. M. A. J.
Mar. 15, 1955, vol. 72

of standardizing hæmoglobinometry and emerged with: (a) a recommended analytical procedure; (b) a simple hæmoglobinometer for general use; and (c) a certified national hæmoglobin standard for distribution to co-operating laboratories.[11, 13, 14, 15]

In the United States the initiative was taken by the Army Medical Service Graduate School with a limited field trial[2] of a cyanmethæmoglobin solution proposed by Dr. David L. Drabkin. The success of the Army plan so impressed the Hæmatology Study Section of the National Institutes of Health that it requested the National Research Council to explore the possibility of establishing a National Hæmoglobin Standard for general use throughout the country.

To this end the Academy-Research Council established an *ad hoc* panel under the Subcommittee on Blood and Related Problems of the Division of Medical Sciences. This panel has sought the cooperation of the College of American Pathologists, the American Society of Clinical Pathologists, the American Association of Blood Banks, the Department of Defence, the Veterans' Administration, the National Institutes of Health, and the National Bureau of Standards. It has also maintained close liaison with the Committee on Hæmoglobinometry of the Medical Research Council of the United Kingdom and with the National Research Council of Canada.

The panel gave serious consideration to the British plan, but decided that, in respect to simplicity and adaptability, the cyanmethæmoglobin method[1, 8, 9, 12, 17, 18] adopted by the U.S. Army would be more suitable for use in the United States and Canada. It was agreed that the choice of a solution of some form of hæmoglobin as a standard for hæmoglobinometry was both logical and direct. In contrast to a glass standard, it would have the advantage of adaptability to a variety of photometric instruments and cuvettes. Among the forms of hæmoglobin well adapted to photometry, cyanmethæmoglobin has outstanding advantages. It has been shown that solutions of this pigment are stable for years when preserved at refrigerator temperatures.[3] The absorption band of cyanmethæmoglobin in the region of 540 mμ is broad rather than sharp, so that its solutions are suitable for use in filter type photometers as well as in narrow band spectrophotometers.[7, 8] Finally, all forms of hæmoglobin likely to be found in blood, with the exception of sulphhæmoglobin, are quantitatively converted to cyanmethæmoglobin upon the addition of a single reagent.[8]

RECOMMENDATIONS

On the basis of these considerations, the panel reached agreement on the following recommendations:

1. There shall be a Standard of Reference in the form of a preparation of crystalline human hæmoglobin prepared by the method of Drabkin.[4, 5, 6] The acceptable criteria for this preparation shall be that a solution containing 1 milliatom of hæmoglobin iron per litre shall have millimolar extinction coefficient of 11.5 at a wavelength of 540 mμ, when measured as cyanmethæmoglobin.[7, 8] Certification of this Standard of Reference shall rest upon the results of spectrophotometric measurements and of analyses for iron made independently by the National Institutes of Health, the Army Medical Service Graduate School, the National Bureau of Standards, and Dr. Drabkin's laboratory at the University of Pennsylvania. Professor King of the Postgraduate Medical School in London, England, will also characterize the Standard of Reference both chemically and spectrophotometrically and compare the results of its use with those of hæmoglobin determinations employing the British standard.
2. The iron content of hæmoglobin shall be accepted to be 0.335%.[10] This value for iron is the traditional figure used in this country and is in substantial agreement with that adopted by the British. It corresponds with an equivalent weight for hæmoglobin of 16,700 per atom of iron and with an oxygen capacity of 1.34 ml. per gram of hæmoglobin.[10]

   The adoption of an agreed figure for the iron content is necessary in order that the spectrophotometric measurements in terms of iron may be translated into grams of hæmoglobin. Should any change be made in the future in the accepted values for the extinction coefficient of cyanmethæmoglobin and the iron content of hæmoglobin, results based on the use of the above standard may be readily recalculated.
3. There shall be a Standard for Distribution in the form of a certified solution of cyanmethæmoglobin which shall be prepared directly from the Standard of Reference. The Standard for Distribution shall be packaged as three separate solutions containing certified concentrations of approximately 20, 40 and 60 milligrams of hæmoglobin in the form of cyanmethæmoglobin per 100 ml.

   These three solutions will correspond to 1 to 250 dilutions of blood containing approximately 5, 10 and 15 grams, respectively, of hæmoglobin per 100 ml. After bottling, samples of these standard solutions will be spot-checked for correctness of optical density by the four analytical laboratories that have been designated above. The batch will then be certified and distributed to co-operating laboratories by designated national agencies.
4. In conjunction with the use of the proposed standards, it is recommended that clinical laboratories consider the adoption of the cyanmethæmoglobin method of hæmoglobin determination described by Drabkin.

   The use of the cyanmethæmoglobin method follows from the concept that it would be logical to adopt a method of analysis which converts hæmoglobin into the same pigment as that used in the standard. It does not, however, preclude the use of the cyanmethæmoglobin standard for the calibration of other methods of hæmoglobin analysis which may be in routine use in some laboratories. However, it should be realized that such a procedure may lead to some loss of accuracy.

   The cyanmethæmoglobin method employs a single solution containing potassium ferricyanide and potassium cyanide, which converts the hæmoglobin in blood quantitatively to cyanmethæmoglobin. The ferricyanide converts the hæmoglobin iron from the ferrous to the ferric state to form methæmoglobin, which then combines with potassium cyanide to produce the stable pigment cyanmethæmoglobin. These two reactions are rapid and stoichiometric.

   There should be no reluctance to employ this standard and reagent because they contain cyanide. The concentration of cyanide in the reagent that is proposed for use is only 52 mg. of potassium cyanide per litre. Its lethal dose for man approaches four litres.[16] Most clinical laboratories use for the determination of uric acid a reagent containing 50 grams of this salt per litre. In view of this and of the fact that laboratories of clinical pathology are disciplined in the use of such dangerous materials as isotopes and virulent pathogens, it would seem that the handling of the proposed reagent constitutes a quite negligible hazard.

The panel also agreed to undertake a field trial of one year's duration using the Standard for Distribution described above. It is now felt that the plans for this field trial have progressed to the point where the participation of laboratories desiring to co-operate may be invited. The standards will be prepared by Dr. David L. Drabkin, and distributed without charge to clinical laboratories on application, provided they will agree to meet certain minimum requirements for participation, as follows:

1. To conduct and report at three-month intervals, for one year, measurements of the actual photometric readings of the three standard solutions in the photometer routinely in use for hæmoglobin measurements in that laboratory.

2. To co-operate in answering a simple questionnaire designed to furnish information on the influence of various factors on the results of the hæmoglobin determinations which will assist the panel in its long-range plans for making this standard available on a national scale.
3. To co-operate in the analysis and reporting of (a) an unknown solution of cyanmethæmoglobin, and (b) an unknown sample of blood.

The Standard for Distribution, consisting of the three solutions described above, will be packaged as a single unit. Details of the procedure for the determination of hæmoglobin as cyanmethæmoglobin, as well as details of the procedure for calibrating another method in terms of the cyanmethæmoglobin standard, will be furnished with the standard.

Distribution will be made to civilian laboratories by the College of American Pathologists, 203 North Wabash Avenue, Chicago, Illinois; to military and government laboratories by the Army Medical Service Graduate School, the Navy Bureau of Medicine and Surgery, the Air Force Surgeon General's Office, and the Veterans' Administration; and *to laboratories in Canada through the Division on Medical Research, National Research Council, Ottawa, Ontario.* Cooperating laboratories are requested to apply to the distributing agency with which they are most closely associated. Because of limitation in the number of sets of the standard available, distribution will be determined by priority of application and willingness to comply with the conditions listed above. Application for standards will assume acceptance of these conditions.

It is estimated that the Standard will be ready for distribution by April 15, 1955.

This plan has been drafted by the *ad hoc* panel on the establishment of a hæmoglobin standard of the Division of Medical Sciences, National Academy of Sciences—National Research Council.

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AN EXTRAPYRAMIDAL SYNDROME WITH RESERPINE*

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THIS PAPER REPORTS the appearance of extrapyramidal signs and symptoms, ranging in severity from cogwheel rigidity in the upper limbs to a state resembling a complete Parkinson syndrome, in 12 of 19 patients receiving the rauwolfia alkaloid reserpine. The patients receiving the drug consisted of 11 women and eight men. Of those developing the extrapyramidal symptoms, nine were women and three were men. The patients ranged in age from 19 to 61.

No other medication or physical treatment was given with reserpine or at the time these symptoms developed. None of the patients showed any initial liver malfunction as measured by the blood alkaline phosphatase level. Of those developing extrapyramidal symptoms, seven had received no other medication before, one had had chlorpromazine four months previously, and four had had electro-convulsive therapy before receiving reserpine. Examination of all patients at the start of reserpine treatment gave no evidence of neurological impairment.

With regard to *dosage*, the amounts of reserpine administered before the appearance of the extrapyramidal symptoms varied considerably from one patient to another. All patients were started routinely on an initial daily dose of 5 mgm. intramuscularly and 3 mgm. orally. This dosage was subsequently adjusted upwards or downwards, depending upon the clinical status of the patient. The amounts of reserpine given thus ranged from 3 to 13 mgm. intramuscularly and from 0.5 mgm. to 5 mgm. orally, daily over the period of treatment. The total amount of reserpine administered intramuscularly and orally before the appearance of cogwheel rigidity was between 21.5 and 193.0 mgm. The total amount administered before the appearance of the Parkinson syndrome was between 54.0 mgm. and 339.5 mgm. All but one patient were on combined intramuscular and oral administration. In this one instance the extrapyramidal signs and Parkinson picture appeared while the patient was on oral administration, receiving 5 mgm. daily for 11 days.

The *duration of treatment* before the appearance of cogwheel rigidity was between three and 19 days, and, before the more complete extrapyramidal syndrome, between 10 and 23 days. There is thus a very wide range of individual

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Canad. M. A. J.
Mar. 15, 1955, vol. 72

difference in the relationship between the appearance of signs and the dosage and duration of treatment.

The first symptom to appear is cogwheel rigidity in the upper limbs, followed by loss of facial mobility and expression and appearance of the typical mask-like facies. These signs are then followed by tremor and rigidity in the upper and lower limbs, loss of associated movements on walking, shuffling gait and monotonous voice. Cogwheel rigidity appeared in 12 of the patients, and the Parkinson syndrome in eight of the 12.

These signs are usually accompanied by marked salivation and drooling, by gain of weight and by complaints of increased frequency of urination. It was also noted in all patients developing this Parkinson syndrome that, regardless of the severity of the overt symptoms and despite the appearance of apathy with mask-like facies, they remained in excellent contact, alert and with no gross impairment of intellectual function. By the time the extrapyramidal symptoms had appeared, the characteristic initial period of somnolence had passed off, and in fact the patients tended quite frequently to complain of feeling restless. Though usually definitely less reactive and more "tranquil," they showed none of the mental apathy or lethargy suggested at first sight by the mask-like facies and shuffling gait. Overt alteration of mood tended to be in the direction of mild euphoria with easy smiling and laughing, even with extrapyramidal symptoms. This was frequently associated, however, in quite anomalous fashion, with subjective reports of depression or of "feeling terrible."

The syndrome showed no sign of remission with continued treatment. Instead, it was slowly progressive and increasingly severe, leading to a picture of almost board-like generalized muscular rigidity. It was necessary to alter administration of the drug because of the extrapyramidal signs, which would gradually diminish or disappear. In some cases, it has been possible to reduce the severity of the extrapyramidal signs and to halt their progression by reduction in dosage. Thus, despite those individual differences already noted, there appeared to be a rough but direct relationship between the level of total daily dosage and the appearance and severity of the various signs.

Finally, it should be pointed out that these signs occurred with much larger doses of reserpine than are ordinarily given for other purposes, such as the medical treatment of hypertension. Papers reporting the use of the drug in such cases either do not mention such signs as those described here, or state specifically that the drug is "remarkably well tolerated over prolonged periods of time, and free from toxic or even very serious side-effects."[1] All the cases treated in this series have been acutely disturbed and agitated and presented problems in ward management. The doses used were those required to reduce this overactivity and were up to ten times as large as those used in the treatment of hypertension.[2, 3]

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CLINICAL EXPERIENCE WITH PSYCHIATRIC PATIENTS ON RESERPINE – PRELIMINARY IMPRESSIONS*

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SO FAR, 19 psychiatric patients have been treated with the rauwolfia alkaloid reserpine, and the study is continuing. These patients, all severely disturbed and selected because they presented problems in ward management, were characterized by over-activity, agitation, and anxiety, frequently accompanied by delusions, hallucinations, or severe dissociation. Diagnoses include eight cases of paranoid states, two of undifferentiated schizophrenic reactions, three of dissociated states with hallucinations or delusions, two of severe anxiety reactions, and one case each of hysteria, barbiturate addiction, depression and psychopathy. There were 11 women and eight men, ranging in age from 19 to 61.

Dosage.—The initial routine dosage is 5 mgm. intramuscularly and 3 mgm. orally, daily, in divided doses of 2.5 mgm. intramuscularly and 1 mgm. orally. This dosage was subsequently adjusted according to the clinical state of the patient, the daily dosage varying over the total period of treatment for all patients between three and 13 mgm. intramuscularly and between 0.5 and 5 mgm. by mouth, giving an average daily maintenance dose of 7 mgm. intramuscularly and 3 mgm. orally.

Duration of treatment.—The duration of treatment ranged from six to 35 days. This has not depended solely on symptomatic improvement but also upon other factors, such as the appearance of side-effects or toxicity, or upon the failure of the patient to show some reduction in activity.

*From the Allan Memorial Institute, Royal Victoria Hospital and McGill University, Montreal, P.Q. The material used was in the form of Serpasil-Ciba, provided through the courtesy of Dr. C. Walter Murphy of Ciba Company Ltd., Montreal.
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Side-effects.—The principal characteristic side-effect that develops is the *extrapyramidal syndrome* which is described elsewhere in this issue. Besides this syndrome, there are a number of other regularly occurring side-effects. These include the following:

1. *Somnolence* has been the characteristic initial reaction of all patients except one woman who had been a barbiturate addict. The somnolence occurred within a day or two of the first administration and lasted for three to seven days. Although the patients tended to wish to lie down and sleep at every opportunity, the somnolence was typically one from which the patients were easily aroused. This somnolence did not occur at night, so that the drug was not useful as a night-time sedative or hypnotic.
2. A marked *increase in appetite* was noted in all of the patients but one. Some of the patients became ravenous and all but one gained considerable amounts of weight, one patient gaining 22 lb. in 25 days.
3. *Flushing, chills, and tremor* were observed quite frequently and appeared at various times throughout the period of administration. The regular *hypotensive* effect of the drug upon blood pressure was noted in several syncopal attacks with no other serious effects. Of considerable interest was the occurrence of a *paradoxical hypertension* on two occasions. Increased salivation and drooling was noted in all patients as a later side-effect of drug administration.

Results.—Reserpine had an effect upon the behaviour and emotional reactivity of all the patients. Generally speaking, this effect was a definite reduction in agitated or overactive behaviour, and made patients less troublesome and easier to manage on the ward. Characteristically, there was a general decrease in the intensity of the patients' reactions to stimuli, usually associated initially with somnolence but continuing after the somnolence had passed. The drug produced no specific changes in mental content, except possibly to reduce the severity and frequency of hallucinations, and seemed mainly to reduce the emotional disturbance and concern associated with abnormal mental content.

It could be said, therefore, that all patients showed improvement with administration of the drug. There was no diagnostic specificity to this, however, and this statement of improvement must be interpreted in the light of our primary objective, which was to reduce overactivity, agitation and severe emotional disturbance, regardless of the diagnosis. As far as underlying personality problems, conflicts and content were concerned, there was no evidence that the drug itself had any direct or lasting effect. When administration of the drug was interrupted, some of the patients returned to their previous symptomatic state while others maintained their symptomatic improvement and continued to improve further. The important question appeared to be whether additional therapeutic activities had been provided while the drug was being administered.

We have been able to identify two possible kinds of additional activity required. The first consists of the patient's own activities toward recovery* which may be postulated as coming into play as the drug serves to interrupt a symptom pattern which has become chronic, oscillating or autonomous.†[1] The second consists of active psychotherapeutic intervention by the psychiatrist, both in terms of the patient's personality structure and in terms of dealing with problems in the patient's family and social situation.

In summary, the drug is definitely useful in reducing the acuteness and severity of problems created on a psychiatric ward by overactive and disturbed patients, both for the patient's symptomatic improvement and for the ward environment. It makes it possible to observe the patient for a longer period for diagnostic formulation without resorting to more strenuous forms of physical treatment or restraint, such as electroconvulsive therapy. At the same time, it is our feeling that the drug, in itself, has no lasting therapeutic effect, but allows time for diagnosis and a therapeutic regimen to be established, and also for spontaneous remission where this is at all possible.

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*"The line between the spontaneous forces tending to recovery—what used to be called *vis medicatrix naturæ*—and the effects of the physician's 'intervention' is impossible to draw with precision in a very large proportion of cases." "Social Structure and Dynamic Process: The Case of Modern Medical Practice" *in: The Social System*, by T. Parsons, Glencoe, Illinois; The Free Press, 1951, p. 449-450.

†This oscillatory behaviour is one of the principal difficulties of a feed-back system. See, e.g., Tustin, A.: *Sc. Amer.*, 187: 48, 1952.

PREVENTION AND CURE

It is well to clarify the meaning of the word "prevention" when used in speaking of "levels of prevention." Dr. Mather of British Columbia has pointed out that in this context the word is used with the meaning it had in Elizabethan times when "prevent" meant to come before or precede. Two examples from the King James Version of the Bible illustrate this use:

> Psalm 88:13—"But unto thee have I cried, O Lord; and in the morning shall my prayer prevent thee." The revised version reads, "But I, O Lord, cry to thee; in the morning my prayer comes before thee."
>
> Psalm 119:147—"I prevented the dawning of the morning, and cried." The revised version reads, "I rise before dawn and cry for help."

Obviously, if we use the word "prevention" only in terms of keeping some possible event from happening, our use of the word is a different one. In this sense, no one is going to try to "prevent" either the Lord or the dawning of the morning. If the meaning is that of anticipatory action, however, anyone practises preventive medicine when he provides the best care available with modern methods, doing all in his power to prevent the progress of the natural history of disease.—H. R. Leavell, *Am. J. Pub. Health*, 44: 1397, 1954.

Canad. M. A. J.
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Editorials

CLINICAL TRIALS

One of the landmarks in medical history is James Lind's clinical trial of oranges and lemons for scurvy in 1747, since it is the first published account of a properly controlled trial of medical remedies. It is true that the British race can take little credit for this, for the results took forty years to penetrate the consciousness of the Lords of the Admiralty. However, of recent years Britain has made ample amends for this by carrying the Lind tradition into national life. A combination of national poverty and national inability to accept without question the findings of foreigners has led to the remarkable development of the special committees of the Medical Research Council whose duty it is to organize tests of particular drugs or modes of treatment.

In a survey of their work, Dr. Green (*Lancet* 2: 1085, 1954) reviews the criteria used in the past to evaluate remedies. He groups them under the headings of *observation, authority* and *experiment*. He recalls that of the thousands of drugs which have been used empirically since the dawn of civilization, few still enjoy a high reputation. Their number includes castor oil, opium, sulphur and mercury. Nevertheless, he emphasizes that "the empirical method, despite its scientific shortcomings, has a number of genuine therapeutic achievements to its credit, and a remedy is not necessarily bad just because it is old and has been evaluated by common experience rather than by critical trial."

We are all aware of the harm done to medicine in the past by the dead hand of authority. Every student knows that the authority of Galen held back progress for centuries, and counts himself fortunate that he lives in an age when ancestor worship is out of date. What he often fails to realize is that authority is still very much with us, but in a more subtle form. Eagerness to share the glad tidings of a new discovery leads prematurely to a press conference or an indiscreet disclosure to a journalist. Radio and television join the press in ensuring immediate worldwide dissemination of the news (and who can blame them?—their job is to present news and not to evaluate scientific work), and we now have the voice of collective authority substituted for the wisdom of the individual. It is doubtful whether the substitution represents a gain.

Turning to experiment, Dr. Green reviews the postwar activities of the Medical Research Council, including the arranging of confirmatory tests on antibiotics and hormones launched upon the American market "with reports which, while sometimes inconclusive, have been sufficiently encouraging to create an urgent demand" in the United Kingdom. The M.R.C. can point with pride to their studies of streptomycin, which provided standards for assessment "not hitherto attained even in America—for the very fact that the drug was so freely available there made it difficult for American clinicians to undertake controlled trials." Their work on resistance of tuberculosis to chemotherapeutic agents, and on the relative merits of cortisone and aspirin, has also been of great importance.

Dr. Green once again makes a plea for the inclusion of the statistician in planning clinical trials and for the withholding from the market by manufacturers of products not yet clinically investigated with statistically adequate controls. Even so, there is a risk of long-term toxic effects which cannot be foreseen. Of recent years we have seen the replacement of innocuous and ineffective symptomatic remedies by really potent drugs. Dr. Green indicates clearly the price that has to be paid for this advance when he says that "a powerful remedy is almost of necessity also in certain circumstances a powerful poison." The long-term hazards can be detected only by the clinician using the new drugs. Every doctor encountering toxic effects has a moral duty to report them, for the scientist conducting group trials can only show the doctor that "the odds are heavily in favour of a remedy being safe when used as directed." More than that the scientist cannot honestly say, for, as a British contemporary sagely remarked, "Science has no bargain basement."

Editorial Comments

L'HÔPITAL D'AUJOURD'HUI

The French-speaking community of North America now has a hospital journal of its own. The Hospital Committee of Quebec has sponsored a new monthly journal, *L'Hôpital d'Aujourd'hui*, which is to be published on the 15th of each month from the offices of the Committee, 325, Chemin Sainte-Catherine, Outremont, Montreal. The first number—January 1955—is a very handsome production indeed, and there is every indication that the new periodical will most satisfactorily fill a gap in the medical literature of this continent.

The direction of the journal is in the very capable hands of Father Hector-L. Bernard, well known in C.M.A. circles as an active member of the Canadian Commission on Hospital Accreditation. The long list of executive staff and consultants inspires every confidence and makes it almost superfluous to wish this new publication every success. There is undoubtedly a need for this journal. In his first editorial, the new editor, Mr. Jean-Paul Martin, refers to the "humble group of French, lost like an island in the immense human sea of America." These are modest words; the group of our French-speaking colleagues is by no means lost or overlooked. Their contribution to the relief of human suffering is great and ever-increasing; it is quite likely that the new journal will exercise an influence in circles far removed from the Province of Quebec.

FLYING SAUCERS

Towards the end of the last century the French psychiatrist, J.-P. Falret, described "délire à deux" in which a delusion is communicated from a psychotic subject to another member of the family. By extension this situation may involve more members of a family, so that, for example, a whole family may assert that they are the victims of witchcraft. From this, it is only a step to the Salem witches, or the devils of Loudun.

Heuyer[1] recently discussed at a meeting of the Académie Nationale de Médecine in Paris the latest manifestation of a collective psychosis which has spread far beyond the confines of family or community. For the witches of Salem, twentieth-century man, with his head full of ill-digested pseudoscience, has substituted the flying saucers. Our modern methods of mass communication, quite impartial in the dissemination of truth or nonsense, have ensured a world-wide propagation of the delusion. We are now all one family, so we are all entitled to share in a psychotic family situation. The nature of the delusion is of interest. We are too knowledgeable and too civilized to be led astray by tales of witchcraft or even Santa Claus, but there is nothing childish or shameful in believing in invaders from another planet.

Heuyer points out that for successful propagation of a collective psychosis, three elements are necessary: (1) a false idea; (2) fear; (3) certain conditions in the group and its environment. The false idea stems no doubt from certain visual phenomena well known to astronomers. For example, one report described the descent and disappearance of a flying saucer at precisely the time at which the planet Venus descended and disappeared. The element of fear is certainly there. Anxiety is never far from the human mind, and all the best delusions thrive on the enjoyment we derive from being frightened. For example, the Loch Ness monster is a monster and not a benign submarine animal. If he were benign, he wouldn't rate a line of newsprint. Similarly, the flying saucers are malignant. We pay our brothers on the other planets the doubtful compliment of supposing them human enough to want to destroy anything strange at sight.

The conditions in the human group could scarcely be more favourable for propagation of a psychotic idea. Within the last few decades, we have discovered so much that even the most sceptical may be forgiven for substituting emotional acceptance of a new idea for scientific proof. From the practical point of view, it probably does not matter much whether people believe in flying saucers or not, except that there is on record the case of a man who was shot at because someone mistook him for a Martian. It is of great interest, however, to find out why certain ideas take root and spread. Studies of group delusions are under way on a small scale here and there. Perhaps somebody like UNESCO could co-ordinate them and even show us how to substitute benign ones for malignant.

1. HEUYER, G.: *Bull. Acad. nat. méd.*, 138: 487, 1954.

NEW DRUGS FOR RADIATION SICKNESS

Swedish observers[1] have published a preliminary communication on the good effects of batyl alcohol in leukopænia due to radiation. It was claimed in 1949 by Sandler that batyl alcohol, which is present in yellow bone marrow, protected animals against benzene poisoning. Edlund now describes experiments showing that in certain circumstances this alcohol had a beneficial effect on radiation injury in mice. Brohult and Holmberg have used the alcohol and certain of its esters to treat 36 cases of leukopænia due to x-irradiation. Of these, 25 responded to treat-

1. *Nature, London*, 174: 1102, 1954.

Canad. M. A. J.
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ment by an immediate increase in the white-cell count. In nine cases there was no further fall in the count after starting treatment. This line of research appears to be promising, and it may even be found that this alcohol and its esters are of use in protecting the blood-forming tissues against damage by x-rays.

THE USE AND ABUSE OF REST

Rest, whether for short or prolonged periods, may be a double-edged sword in the treatment of patients with injury or disease. Prior to modern therapies rest was often the only treatment available, and it is only in recent years that the dangers of rest have been recognized. The population continues to age, and the care of the aged is becoming an increasingly important social matter. Various authorities have reported the serious effects on the elderly patient when put to bed.

Often due to shortage of nursing staff the elderly person with minimal arteriosclerotic or locomotor defects is placed in bed with disastrous results. He or she becomes dependent on the attendants for all bodily and mental needs with resultant stagnation: urinary and bowel incontinence, or mental and physical inertia result from such enforced rest in bed. Anderson[1] has recently described the genito-urinary aspects of prolonged decubitus with particular reference to calculus formation: he states that much can be done for bedridden senile patients with incontinence. If they are coaxed out of bed and reassured they may well be on the way to being cured of their incontinence.

The emancipation from prolonged bed rest of the patient with a stroke is an excellent step, but it must not be forgotten that if the patient is put to bed for even a short period his position in bed is most important. Rest in bed without attention to movements of shoulder and leg will result in stiffness requiring months of rehabilitation. The same principles are applicable to all classes of patient and exercises for feet, legs, and spinal muscles are a necessary daily task for the bedridden patient.

Wells[2] has recently pointed out that the best example of discarding rest is the throwing overboard of the Fowler position for fear of deep venous thrombosis of the legs. Instead of a continuous comfortable propping up in bed after an operation, the patients are made to lie flat for ten minutes daily with active and passive exercises for feet, legs and respiratory muscles. Early ambulation with visits to the toilet or commode have replaced the continuous bed rest and bed pan for the postoperation patient.

In spite of or perhaps because of antibiotics, rest remains the mainstay of treatment of tuberculosis, but as in other chronic disease physical rest is not enough; peace of mind is an essential for the successful treatment of the tuberculous as well as other patients. Physical rest remains an essential part of the treatment of rheumatoid arthritis, sciatica, and fractures, but must be associated at the same time with intelligent physiotherapy. Above all, rest of the mind remains paramount, and the effect of visitors at the patient's bedside may disturb such tranquillity. In conclusion let us not forget Mark Twain's observation on how many more people die in their beds than when travelling by train: "Don't take any more chances in those beds, the railroads are good enough for me." W.F.T.T.

1. ANDERSON, H. F.: *Postgrad. Med. J.*, **30**: 15, 1954.
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RETROLENTAL FIBROPLASIA

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There is considerable experimental evidence to show that a high oxygen concentration is a definite factor in the production of this condition. Gyllensten and Hellström[2] showed that intermittent exposure of newborn mice to 100% oxygen for a few weeks resulted in hæmorrhages into the vitreous body, hyperplasia of the tunica vasculosa lentis and detachment of the retina. Gordon et al.[3] have commented on the increase of retrolental fibroplasia noted when premature baby units were moved to new quarters where a piped-in oxygen supply made oxygen therapy easily available. These authors found that concentrations of oxygen over 50 to 60% were being given to premature babies: and that the incidence of retrolental fibroplasia dropped virtually to nothing when the concentration of oxygen in incubators was dropped to only 30 to 40%. It was also found that the survival rates of infants were relatively unaffected by the reduction in oxygen concentration.

Gordon *et al.* suggests that the degree of prematurity, and possibly other factors may also play a part in the production of this disease. Their findings are more than of academic interest and confirm the work of other authors in this field. W.F.T.T.

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Men and Books

BISHOP'S MEDICAL COLLEGE*

E. H. BENSLEY, M.D., *Montreal*

HISTORICAL ACCOUNTS of the medical schools of Montreal assign the leading roles to the Montreal Medical Institution, L'Ecole de Médecine et Chirurgie de Montréal and the university faculties to which they gave birth. It could hardly be otherwise. The Montreal Medical Institution, founded in 1823, became within a few years the Medical Faculty of McGill University. The French School, founded in 1843, had a more stormy course but triumphed in the end. After an uneasy affiliation with Victoria University, a Methodist college in Cobourg, Ontario, L'Ecole established a connection with Laval and finally became the Medical Faculty of the University of Montreal. But there have been other medical schools in Montreal. The most successful of these was Bishop's Medical College or, to use its full name, the Medical Faculty of the University of Bishop's College. Notable contributions to medicine were made by this School. Its story deserves more attention than it has received.

Bishop's Medical College was founded in 1871. As an English-speaking school and a rival of the McGill Medical Faculty, it played an active and prominent part in medical education for 34 years. In 1905 it lost its separate identity through merger with the Medical Faculty of McGill University. Although the parent institution, the University of Bishop's College, was and still is at Lennoxville in the Eastern Townships of Quebec, the Medical Faculty was always in Montreal. The first session of 1871-72 was held in rented rooms at McGill and Notre Dame Streets. The following year the College moved into a new building of its own on the north-east corner of St. George (now Jeanne Mance) and Ontario Streets. All subsequent sessions were conducted there. This building still remains but has long since been converted into stores and apartments.

For clinical teaching the School was affiliated with the Hôtel-Dieu, the Montreal Dispensary, and the Montreal General, Royal Victoria, Western and Woman's Hospitals. Its connections with the last two were especially close. Bishop's actively supported the establishment of the Western Hospital, now the Western Division of the Montreal General Hospital. When the oldest part of the Western Hospital, the Mills Building, was demolished a few months ago (1954), one of the items found in the cornerstone was a copy of the Annual Announcement of Bishop's Medical College for 1876-77. Most of the physicians and surgeons of the Western Hospital held teaching appointments in the Bishop's School. The Woman's Hospital, now in greatly expanded form the Reddy Memorial Hospital, was under the direct management of Bishop's Medical School. Its physician accoucheur, Dr. Herbert Reddy, was Professor of Obstetrics.

Two hundred and forty-six men and women obtained their degrees of M.D. and C.M. from Bishop's School—a substantial number for those days. The list of graduates contains many well-known names. Three are selected for mention because they will be immediately familiar to members of this audience: Casey A. Wood, a noted ophthalmologist whose name is perpetuated at McGill in the Wood Gold Medal and the Wood Library of Ornithology; William Henry Drummond, famous for his poetry in the habitant dialect but also a distinguished physician; and Maude Abbott, whose contributions to medicine and to McGill are a matter of common knowledge.

Two special achievements of Bishop's Medical School remain to be mentioned—the admission of women and the creation of a dental department. In 1890, Bishop's took the advanced step of admitting women to its medical school on an equal footing with men. This was a bold experiment. At that time many experienced teachers at McGill and elsewhere were strongly opposed to co-education in medicine. In 1896, a Department of Dentistry was formed in the Faculty of Medicine by affiliation of the Quebec Dental College with the University of Bishop's College. Teaching was in both French and English. Bishop's thus became the first university in the Province of Quebec to provide a dental course leading to the degree of Doctor of Dental Surgery.

This record of achievement is in itself sufficient justification for the creation of a new medical faculty in a city which already had two medical schools. But it is of interest to inquire more closely into the reasons for the formation of this School in 1871 and also to determine the cause of its sudden disappearance from the scene in 1905 after 34 years of active life.

The story of Bishop's Medical College is, to a large extent, the story of the ambition and effort of one man—Francis Wayland Campbell. Dr. Campbell was one of the founders of the College. He was its first registrar and later became its dean, in addition to holding a number of teaching appointments. Dr. Campbell entered practice in Montreal in 1862. His interest in medical education became evident at once. By 1864, he and Dr. G. E. Fenwick had launched a new journal—the *Canada Medical Journal and Monthly Record of Medical and Surgical Science*. Dr. Campbell was ambitious, energetic and able. He was not a member of the staff of the McGill Medical School. He wanted a more active part

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in educational work and deeply resented what he regarded as the monopoly of medical teaching, hospital appointments and even private practice held by the medical staff of McGill.

He was not alone in his views nor were his views new. We are told that even L'Ecole de Médecine et Chirurgie de Montréal, ostensibly founded to meet the needs of French-speaking Canadians, was established in protest against what was then considered the monopoly of teaching privileges and of appointments at the Montreal General Hospital by those in authority at McGill. Support for this statement is found in remarks made by Dr. William Sutherland in his opening lecture at the French school in 1844. Speaking of the McGill Medical School, he said:

"What exclusive right is possessed by this Faculty? What species of idolatry is it which sought to enforce us to blindly worship the memory of its departed founders, in permitting their representatives to hold within an iron grasp all the reputation derivable from such a source? What has rendered this place a shrine at which they alone are to receive homage?"

Many years later, Dr. Campbell quoted these words with obvious approval. It is clear that the feeling grew stronger with the passage of time, until in 1871 it culminated in the formation of Bishop's Medical College. It would be pleasant to relate that bitterness was now replaced by friendly competition and mutual respect. But such was not the case. Evidences of more kindly feelings are to be found here and there, especially in accounts of formal occasions, such as banquets, convocations and funerals. But the record shows that rivalry remained bitter, moderating only after the turn of the century.

Reference has been made to the medical journal edited by Dr. Campbell and Dr. Fenwick. Within a year after the opening of the Bishop's School, the editorial partnership was dissolved and the journal discontinued. In its place there appeared two journals—the *Canada Medical and Surgical Journal*, edited by Dr. Fenwick and others of the McGill School, and the *Canada Medical Record*, edited by Dr. Campbell and others of the Bishop's School. One of the planks in the platform of the *Canada Medical Record* was declared to be "opposition to monopolies which unfortunately exist in the Professional as well as in the Mercantile world." Addresses and articles by protagonists of Bishop's reveal the temper of the times. Two quotations are selected as typical.

"The narrow-minded and illiberal partizans of other schools predicted failure on our part, and judging us by their own standard, slandered the capabilities of our professors."

"Has a medical school with such a record as this, no claim to have some of the hospital honours fall to its lot? If McGill can prevent it she will. Her history from her foundation has been one of monopoly. She has tried by every means in her power to crush Bishop's Medical College but unsuccessfully."

This second quotation is taken from an editorial written in 1891, when Bishop's Medical College was 20 years old.

Knowledge of this bitter rivalry is necessary to an understanding of those times. But it must be viewed in proper perspective. No doubt right and wrong were to be found on both sides. Equally certain is it that both sides commanded the services of able and self-sacrificing men, devoted to the best interests of medicine. It is probable that the rivalry spurred Bishop's to greater efforts and that Dr. Campbell and many of his associates enjoyed a good fight. The tributes paid to Dr. Campbell, when his day of sorrow and grief came, showed that he was held in great esteem by many outside the Bishop's circle. He was styled by his contemporaries the leader of the medical opposition in Montreal and it was said that he counted among his best personal friends his most bitter political enemies.

I have spoken of Dr. Campbell's day of sorrow and grief. It came in 1904. In that year, he lost his elder son. In April of the following year, ill health forced him to resign the deanship of his beloved school. The same month of April saw the loss of his only surviving son. In May, Dr. Campbell himself succumbed to his fatal illness.

With the death of Dr. Campbell, Bishop's Medical College lost not only a dean but also its staunchest supporter. The college faced serious difficulties. The faculty required reorganization under a new dean, increased financial support was urgently needed and enlarged hospital facilities and college buildings had to be obtained. Bishop's took stock. It heeded advice given by Osler two years before in an address delivered in Toronto on the occasion of the merger of the medical faculties of the University of Toronto and Trinity University. Osler said:

"The day has passed in which the small school without full endowment can live a life beneficial to the students, to the profession or to the public. I know well of the sacrifice of time and money which is freely made by the teachers of those schools; and they will not misunderstand my motives when I urge them to commit suicide, at least so far as to change their organizations into clinical schools in affiliation with the central university."

Osler's remarks applied to Bishop's Medical School, and, in 1905, it joined the Medical Faculty of McGill University. In so doing, it sacrificed its separate identity. This was a wise and unselfish act.

"To Bishop's, McGill brought the advantages inseparable from a larger and more powerful school. To McGill, Bishop's brought a band of devoted teachers and practitioners, who, having been tried in the furnace of adversity, had not failed, but had earned the respect of professional colleagues, who at one time had not regarded the new School too favourably."*

*This quotation is taken from the history of the Western Hospital. Its author is unidentified; probably it was the late Mr. R. C. Fetherstonhaugh.

It is perhaps unnecessary for me to remind you that, although its medical school ceased to exist in 1905, the parent body in Lennoxville—the University of Bishop's College—has continued to serve the cause of education in other ways. Basing its academic tradition on a strong Christian faith, awareness of the importance of the humanities, and recognition of the role of science in the modern world, Bishop's University has grown steadily over the years. In 1945 it observed its hundredth birthday. In 1953 it celebrated the hundredth anniversary of the granting of its Royal Charter by Queen Victoria. Dr. D. C. Masters, Professor of History at Bishop's, has written an account of the first hundred years. In it he states that the story of the medical faculty is a bright, although sometimes forgotten page in the history of Bishop's University. I hope that my story has shown that the page, although not without its bitterness and tragedy, is bright indeed and deserves to be remembered with gratitude and pride.

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GENERAL PRACTICE

INTERNSHIP TRAINING FOR GENERAL PRACTICE

Report of the Committee on Internship Training of the College of General Practice

THE COLLEGE of General Practice of Canada is pressing for more than the usual one-year rotating internship as preparation for general practice. It advises a second year. However, in urging our prospective general physicians to take another year's hospital training the College feels the internship training must be different from that leading to a specialty. It has serious misgivings about some of the features of another year of formal training in teaching hospitals.

The Committee on Internship Training of the College has given considerable thought to the type of internship required for general practice, and from its discussions several conclusions seem justified.

A second year of internship would provide additional experience and responsibility in those branches of medicine which are of primary importance to the general practitioner.

The Committee on Internship Training for General Practice introduces the following recommendations:

1. That hospitals having internship training facilities and training programmes provide special training for doctors planning to enter general practice.
   (a) That the usual first year rotating internship be required.
   (b) That a second year internship or residency be arranged to provide the following subjects or their equivalent:
      (1) Three months medicine, including dermatology.
      (2) Three months obstetrics and gynæcology.
      (3) Three months general and emergency surgery and fracture work, ENT surgery, and urology.
      (4) One month anæsthesia.
      (5) Two months pædiatrics. If unavailable, four months each in medicine and obstetrics and gynæcology.
   (c) That a preceptorship programme be included or follow immediately.
   (d) That the second year be recognized as a residency or assistant residency, and that a suitable certificate be presented to the trainee for satisfactory completion of the training.

Although this specific programme is outlined, it is to be considered flexible, depending upon the special needs of the individual and the community in which he intends to practise. For instance, in some large cities much less surgery is being done by the general practitioner than formerly, whereas in the rest of Canada he will continue to do much of the surgery. This raises the question whether regulations for a second year internship should be on a national or sectional basis, to meet the varying needs of the different parts of the country.

It was agreed that preceptorship experience is one of the best introductions to the work of general practice. By working with a busy senior general practitioner, the intern would learn not only more of the practical application of his techniques, but also how to set up and conduct an office, and how to deal better with patients in the office and in their homes. It was felt that

Canad. M. A. J.
Mar. 15, 1955, vol. 72

POSTGRADUATE COURSES SUITABLE FOR GENERAL PRACTITIONERS
COMPILED BY THE COMMITTEE ON EDUCATION OF THE COLLEGE OF GENERAL PRACTICE

Type	*Sponsored by*	*Location*	*Usual date*	*Length*	*Cost*
Psychiatry	Dalhousie University	Victoria Gen. Hospital Halifax	Jan. 31 - Feb. 1	2 days	$10.00
Medicine	" "	" " "	Feb. 28 - Mar. 4	one week	$5.00 per day
Anæsthesia	" "	" " "	Mar. 28 - Mar. 31	4 days	$5.00 per day
Surgery	" "	" " "	Apr. 25 - Apr. 29	one week	$5.00 per day
Obstetrics, gynæcology, and pædiatrics	" "	" " "	May 16 - May 20	one week	$5.00 per day
Refresher course	" "	" " "	October	5 days	
Extra-mural courses	New Brunswick Medical Society		about 10 yearly		
P.E.I. Medical Ass'n annual meeting		Charlottetown, P.E.I.		6 hours	
Varied individual lectures by visiting speakers		Charlottetown, P.E.I.		6 hours yearly	
Many postgraduate courses available in Boston and the New York Polyclinic					
	West Coast Medical Society and Postgraduate Dept., Dalhousie U.	Corner Brook, Nfld.	2nd week May	1½ days	0
	Central Nfld. Clinical Society and Postgraduate Dept., Dalhousie U.	Grand Falls or Gander	2nd week May	1½ days	0
	Nfld. Division C.M.A. and Postgraduate Dept., Dalhousie U.	St. John's	September	1½ days	0
	(Held immediately prior to annual convention)				
Varied	Hamilton Academy	Hamilton	q. Wednesday	2 hours	$2.00
Varied	Buffalo Academy	Buffalo	q. Wednesday	2 hours	
Surgery and radiology	Sunnybrook Hospital	Toronto	Oct. 28, 29/54		
Pædiatrics	Sick Children's Hospital	Toronto	Nov. 8, 9, 10/54	18 hours	$10.00
Cancer	Cancer Society and Ontario Medical Association	Sunnybrook Hospital Toronto	April 18, 20/55		
Refresher course	Queen's University	Ottawa Civic Hospital	May 23, 24/55		
Refresher course	St. Michael's Hospital	Toronto	Feb. 24, 25, 26/55		$15.00
Refresher course in pædiatrics	Children's Memorial Hospital	Montreal	Mar. 31 - Apr. 2		
Applied physiology	Dept. of Physiology and Med. Research of Faculty of Medicine	Winnipeg	Jan. 3 - Apr. 4/55	3 months	$50.00
Obstetrics and gynæcology	Faculty of Medicine	Winnipeg	Apr. 4-7/55	4 days	$25.00
Surgery for Gen. practice	General Pract. Assoc. of Manitoba	"	Wednesday	Nov. - March	
Convention	Winnipeg Med. Society	"	once a week	30 hours	
Convention	Manitoba Med. Assn.	"	September	5 days—30 hours	
Obstetrics, medicine, surgery pædiatrics, anæsthesia	Postgraduate Committee Vancouver General Hospital	Vancouver, General Hospital, Vancouver	Spring and Fall	Approx. 3 days each	$15.00
General course (variety)	G.P. Section of B.C.M.A.	Harrison Hot Springs	March	2 days	$10.00
Summer school (variety)	Vancouver Medical Association	Vancouver	June	4 days	$10.00
Travel teams (variety)	C.M.A. - B.C. Division	Rural B.C.	Spring and Fall	2 - 5 hours	0
Numerous courses (variety)	Medical School	Portland and Seattle	variable	1 - 6 days	up to $50.00
Numerous courses (variety)	Cook County Postgraduate School	Chicago	Spring and Fall	2 - 21 days	up to $200.00
C.M.A. - B.C. Division annual convention	B.C. Division, C.M.A.	Vancouver or Victoria	October	3 days	0
General Pathology, physiology	University of Alberta G.P. Association Edmonton	Edmonton Edmonton	annual	10 hours	

The Executive Secretary, College of General Practice, 176 St. George St., Toronto, will be pleased to hear of omissions from the list.

a minimum of one month should be devoted to this, either during the second year internship or immediately following it. The intern would see patients only with the preceptor, and in no sense would he be an assistant or locum tenens. The College of General Practice is prepared to assist with the preceptorship programme.

A number of Canadian hospitals have residencies in general practice. In general we approve of them. We wish to bring them to the attention of interns progressing to general practice. Full details of their training programmes with their payment schedules may be obtained from the director of the programme or from the administrator of the hospital.

We appreciate the help of these hospitals in working out a second year of internship for general practice. We wish to assist them in this. We are also asking all interested hospitals to give us further aid in standardizing this programme.

The following hospitals have residencies in general practice:

1. Postgraduate Committee of Dalhousie University. Four residencies. Intern training includes:
   - 3 months medicine at Camp Hill D.V.A. Hospital.
   - 3 months obstetrics in 2 Charlottetown hospitals.
   - 3 months pædiatrics in Children's Hospital, Halifax.
   - 3 months surgery and minor surgery in New Glasgow hospitals.

   Applications made to: Executive Officer, Postgraduate Committee, Victoria General Hospital, Halifax.
2. Saint John General Hospital, Saint John, N.B. Write to Dr. Carl R. Trask, Director.
3. Hôpital de l'Enfant Jésus, Quebec, P.Q. Senior rotating internships in general practice available. For information write to Dr. C. A. Gauthier, Chairman, Committee on Internship.
4. Hôpital du St-Sacrement, Quebec, P.Q. Senior rotating internships in general practice available. For information write to Dr. R. Lemieux, Medical Director.
5. Royal Victoria Hospital, Montreal, Quebec. Six residencies beginning in June each year. The first and second year's training are planned as one course. Information may be obtained from: Dr. J. Gilbert Turner, Executive Director.
6. Ottawa Civic Hospital, Ottawa, Ontario. A one-year senior rotating internship and a two-year senior rotating internship. Information may be obtained from: Dr. H. Featherstone, Secretary, Intern Committee, Ottawa Civic Hospital.
7. The Peterborough Civic Hospital, Peterborough, Ontario. One resident and 3 assistant residents. Information may be obtained from: Dr. L. J. Calvert, Secretary, Intern Training Committee.
8. Toronto East General and Orthopædic Hospital, Toronto, Ontario. Two residencies. Applications made to: Mr. W. E. Leonard, Superintendent.
9. The General Hospital of Port Arthur, Port Arthur, Ontario. Residencies in General Practice are being considered. Information may be obtained from: Mr. J. A. McNab, Administrator.
10. Regina General Hospital, Regina, Saskatchewan. Residencies available. Applications may be made to: Dr. M. G. Israels, Director, Medical Education, Regina General Hospital.
11. Royal Alexandra General Hospital, Edmonton, Alberta. Residencies available. Information may be obtained from: Dr. D. R. Easton, Superintendent.
12. Calgary General Hospital, Calgary, Alberta. Four residencies in General Practice available. This may be increased. For information write to Dr. L. O. Bradley, Administrator.
13. Holy Cross Hospital, Calgary, Alberta. Residencies in General Practice available. For information write to Dr. John B. Corley, Chairman.

G.P. RESEARCH IN THE U.K.

THE COLLEGE OF GENERAL PRACTITIONERS has issued its fifth research newsletter (*Practitioner*, February 1955) in which emphasis is laid on the value of individual work. There are innumerable clinical impressions to be gained by every family doctor every day; the attempt to discover whether they are based on fact is intellectually satisfying, but the doctor also needs to know whether his observations are new or whether others have made them and explained them satisfactorily. For this he needs help and it is hoped that the College research organization will be able to give him that help. The College maintains that, apart from the possibility of aiding medical progress, the discipline in accurate and critical clinical observation must tend to make any doctor a better doctor, and thus help to raise the standard of practice. The U.K. College of General Practitioners intends to award a Butterworth Gold Medal for research.

Mention is made of the large-scale morbidity survey about to be launched by the College, 100 members of which will supply the material which the Registrar-General's statisticians will analyze. It is hoped to present the Government

Canad. M. A. J.
Mar. 15, 1955, vol. 72

with figures for morbidity of a much greater degree of accuracy than has ever been obtained.

In order to ensure that poor-quality research is not started in the name of the College, local research committees have been set up to obtain protocols of proposed investigations for screening at headquarters. The chairmen and secretaries of local research committees will meet once a year at headquarters.

Group studies in progress deal with infective hepatitis, measles, and respiratory tract diseases. Other projects include an investigation into the natural history of glandular fever, a study of the efficiency of an influenza vaccine, and a study on the effects of attitudes towards marriage, the home, and the family as a factor in marital relationships.

MISCELLANY

THE CHARLES H. BEST INSTITUTE

The Charles H. Best Institute in the University of Toronto is now in use. Located on College Street to the west of the Banting Institute, the building consists of six storeys, including basement and sub-basement. Two university departments are accommodated in the building, the Banting and Best Department of Medical Research and the Department of Physiology. Quarters are provided also for the virus research section of the Department of Bacteriology. In addition to the research and other laboratories there are a conference room, a library, and a lecture theatre accommodating 200 people.

The special laboratories include two cold rooms, one with a controlled temperature range of plus 60° F. to minus 40° F. and the other from plus 60° F. to plus 25° F.; a laboratory with temperature control through 40° F. to 104° F. and humidity control throughout this range of temperature; a soundproof and electrically shielded laboratory; and a constant-temperature room (70° F.), designed to improve histological section cutting during the summer months.

Separate from the building and built out under Queen's Park, with entrances from the sub-basement of the main building, are two sections for special studies. One section houses a cobalt bomb and Maxitron x-ray equipment; the other consists of two laboratories for the preparation and processing of substances containing radio-isotopes, with a special animal room, accessible through the laboratories, for related studies.

Machine shop, electronic section, and research stores are located in the basement. A hoist serves the rear entrance, basement floor and sub-basement, keeping the receiving of supplies, including animals, separate from the main building.

Two surgical operating rooms, a preparation room, a recovery room, and a clinical x-ray room are located in the sub-basement. A large section of the sub-basement under the courtyard accommodates the rat colony. The number of rats, young and adult, in the breeding colony averages 1,200, and about 1,600 animals can be handled in the experimental section. The mouse section consists of 1,000 mice. A separate section provides for the preparation and storage of diets for the animals. Throughout the animal sections the temperature is maintained at 70°-72° F. All the rooms in these sections are ventilated by a negative pressure exhaust system; the animal odours are prevented from escaping through the building, as the drift of air is always into the animal rooms from the corridor. Elevated temperature control in two of the smaller animal rooms makes possible the study of hypophysectomized animals under controlled conditions.

In addition to teaching, the staff members carry on experimental investigations. Dr. Best and Mr. J. M. Salter are studying insulin as a growth hormone. Dr. C. C. Lucas and Dr. J. H. Ridout are working on the biochemistry of lipids and dietary lipotropic factors in rats and guinea pigs. Dr. G. A. Wrenshall is studying extractable insulin of pancreas and other problems of carbohydrate metabolism.

Dr. E. A. Sellars is in charge of work in connection with exposure to cold as well as of studies on the production of tumours of the thyroid and on the effects of irradiation. Dr. J. C. D. Barlow assists Dr. Sellars in the radiation work.

Dr. W. G. B. Castleman is studying a variety of problems in physiological histochemistry. Dr. J. W. Scott is in charge of electronic equipment for neurophysiology. Dr. R. E. Haist is continuing the work on factors influencing the islets of Langerhans and on a number of other problems. Dr. James Campbell is studying further the role of the anterior pituitary in metabolism. Dr. O. Sirek is investigating the role of insulin in the action of other protein anabolic hormones. Dr. B. Rosenfeld is studying phospholipids and choline deficiency. Dr. A. M. Rappaport is investigating the role of the acini of the liver lobule in hepatic physiology and pathology and the production of experimental hepatic coma. Dr. W. J. Linghorne is observing bone growth and repair.

Dr. W. R. Franks is working on experimental cancer, radiation chemotherapy and postmortem detection of hypoxia. Dr. D. W. Clarke is doing electrophoretic analysis and fractionation of protein mixtures as well as conducting other studies on proteins.

The Institute, built at a cost of $2,500,000, was financed by funds from a University appeal, grants from the Federal Government and the Province of Ontario, donations by commercial companies, and private gifts.

LILLIAN A. CHASE

NEW WORDS FOR OLD

Will Osler wrote his classic works, in language clear and simple:
An "epidermal pustule" he was apt to call a "pimple."
We docs today don't write that way: we like to show our lore
By massing polysyllables till they trickle out the door.
"Prior (or previous) to," we say, but never once "before."

Disease "eventuates," not "ends," when stops the halting breath;
And "a fatal termination" takes the place of dusty "death."
But before this the "decedent" has ceased to be a man,
For not a "person" but a "case" fits in our modern plan.
Simplicity, to an M.D., has fallen 'neath a ban.

"Essential," "necessary" acts today are "mandatory";
"Sanguineous" is the word to use for "bloody," "blood-stained," "gory."
If, "ambulating" down the street, we tangle with a cab,
To "quantitate" our blood loss is the function of the lab.
(Such gibberish is never heard, when we just stand and gab.)

These sad "traumatic episodes" have nowadays no "cause,"
Only an "etiology" . . . a word which laymen awes.
We've shed "partial" for "subtotal," and "use" for "utilize":
The jargon of psychiatry merits a special prize . . . .
And Osler groans from Heaven, "Write ENGLISH, d - - n your eyes!"

I. J. PATTON

Association Notes

SOCIAL AND OTHER ACTIVITIES AT THE ANNUAL MEETING

THE PUBLICATION of the Preliminary Scientific Programme for the Conjoint Annual Meeting of the British, Canadian and Ontario Medical Associations in our March 1 issue will have convinced all that an outstanding refresher course has been prepared.

However, the advantages of attending medical meetings include more than postgraduate education, and this announcement is intended to acquaint you with some of the other features of a unique medical gathering.

Tuesday, Wednesday and Thursday, June 14, 15 and 16

The British Commonwealth Medical Conference. This is a small meeting of official delegates from the national medical associations of Great Britain, Eire, Australia, New Zealand, Southern Rhodesia, South Africa, India, Ceylon and Canada. A programme has been prepared to inform those in attendance of certain aspects of Canadian medical problems and to learn from them how similar problems are being handled throughout the Commonwealth.

A day at the Connaught Medical Research Laboratories has been arranged and the delegates will be entertained at luncheons and dinners by representative bodies of organized medicine in this country.

Friday and Saturday, June 17 and 18

The annual meeting of the General Council of the Canadian Medical Association has been advanced to the Friday and Saturday preceding the opening of the scientific sessions. The important work of the Parliament of Canadian medicine must be transacted and it is hoped that this will be accomplished in the time allotted in order to permit the members of General Council to take part in the programme of the subsequent week.

The main body of members of the British Medical Association will arrive in Toronto during the sessions of General Council and their reception will be the responsibility of active local committees. Medical Convocation at the University of Toronto will take place on Friday, June 17, and a number of honorary degrees will be conferred to mark the visit of the British Medical Association.

British Medical Association members and their wives, and members of General Council and their wives, will be guests of Lady Eaton at supper at Eaton Hall Farm, King, Ontario, on the evening of Friday, June 17. On Saturday, June 18, they will be guests at a civic reception and musicale to be tendered by the Mayor and Corporation of the City of Toronto.

Sunday, June 19

At 3.00 p.m. the official religious services will be held; the Protestant service, arranged by the Federation of Medical Women of Canada, will take place at St. James's Cathedral and the Roman Catholic service at St. Michael's Cathedral. All members of the Associations represented at the Conjoint Meeting and their ladies are urged to attend these services.

Private supper parties have been arranged by Toronto hostesses for the entertainment of overseas guests and members of the General Council and their wives.

Monday, June 20

The full-scale scientific programme begins. Outstanding exhibits of medical products will be open for your inspection, the Physicians' Art Salon will be on display, and an interesting scientific exhibit has been arranged.

The Association Luncheon programme will be in charge of the Canadian Pharmaceutical Manufacturers' Association. The presentation of their Medal of Honour will be made to Sir Henry Dale.

At 8.30 p.m. the Adjourned Annual General Meeting of the British Medical Association will be held in the Concert Hall, Royal York Hotel. This is a ceremonial occasion at which Dr. T. C. Routley will be installed as President, and it will be followed by a reception and dance.

Tuesday, June 21

This is Ontario Day. In addition to the continuing scientific programme, the Association Luncheon will feature a speaker representative of the Government of the Province. The Annual Dinner of the Ontario Medical Association will take place at 7.00 p.m. and all those in attendance at the Conjoint Meeting will be most welcome to attend. Entertainment will take the form of a monster square dance. Expert instruction will be available so that novices, as well as experts, can enjoy the hoedown.

A number of class reunion dinners have also been arranged for this evening. The members concerned will have received information from their class executives.

Canad. M. A. J.
Mar. 15, 1955, vol. 72

Wednesday, June 22

The scientific programme of Round Table Conferences, General Sessions and Sectional Meetings proceeds. An Association Luncheon will be held and, as a special feature of the afternoon session, a symposium on the National Health Service in Great Britain will be conducted. The evening function is the Annual General Meeting of the Canadian Medical Association at which the President will be installed, Senior Memberships conferred and delegates from sister medical associations welcomed. This ceremonial occasion will be followed by the President's reception and dancing.

Thursday, June 23

The scientific programme continues full scale. The Association Luncheon will be addressed by the Honourable Paul Martin, Minister of National Health and Welfare. The social highlight of the week is the Annual Dinner of the British Medical Association, to which all the ladies and gentlemen attending the meeting are invited. Guests will include representative Canadian citizens.

Friday, June 24

The scientific programme will conclude at noon to permit members to take part in the Association Golf Tournament, which will be held at the Scarborough Golf Club. An excursion to Niagara Falls has been arranged for our overseas guests through the courtesy of the Hydro-Electric Power Commission of Ontario. The entire party will be transported by buses, with a luncheon stop at the Mountain Sanatorium, Hamilton. Tea at Niagara will be provided by the Niagara Falls Medical Society. After they have viewed the sights, a farewell dinner will be tendered to our guests and the Falls will be viewed under illumination before the party returns by bus to Toronto. A limited number of tickets will be available to Canadian doctors and their wives, and these will be reserved for non-residents of Ontario.

The above represents a summary of some of the social and other events of a crowded week. With the exception of privately arranged dinners and class reunions, all of the ladies and gentlemen registered at the meeting are invited to all of the functions. Tickets for luncheons and dinners will be on sale at the Registration Desk.

A separate and supplementary programme of entertainment for all doctors' wives has been arranged, details of which will be available on registration.

CHRISTIAN MEDICAL FELLOWSHIP

The Annual Breakfast of the Christian Medical Fellowship of Britain will be held in the Palm Court, Royal York Hotel, Thursday, June 23, at 7.45 a.m. (prompt). The chair will be taken by T. Clarence Routley, C.B.E., M.D., LL.D., F.R.C.P.[C.], President of the British Medical Association. The speaker will be John R. Brobeck, Ph.D., M.D., Chairman of the Department and Professor of Physiology, School of Medicine, University of Pennsylvania. All interested doctors in attendance at the Annual Meeting are cordially invited to come to this breakfast.

MEETINGS OF AFFILIATED SOCIETIES

The following Canadian societies have planned their Annual Meetings in relation to the Conjoint Annual Meeting of the British, Canadian and Ontario Medical Associations. In several instances the official participation of their counterparts from Great Britain has been arranged and in all cases the attendance of interested doctors from the United Kingdom will be welcomed.

CANADIAN PÆDIATRIC SOCIETY

Château Frontenac, Quebec. June 15, 16, 17 and 18.

Secretary: DR. J. C. RATHBUN, 526 Waterloo St., London.

CANADIAN OPHTHALMOLOGICAL SOCIETY

Bigwin Inn via Huntsville, Ont. June 14, 15 and 16.

Secretary: DR. R. G. C. KELLY, 90 St. Clair Ave. W., Toronto.

CANADIAN OTOLARYNGOLOGICAL SOCIETY

Bigwin Inn via Huntsville, Ont. June 16, 17 and 18.

Secretary: DR. ARNOLD HENRY, Medical Arts Bldg., Toronto.

SOCIETY OF OBSTETRICIANS AND GYNÆCOLOGISTS OF CANADA

Bigwin Inn via Huntsville, Ont. June 17, 18 and 19.

Secretary: DR. F. P. MCINNIS, 280 Bloor St. W., Toronto.

CANADIAN NEUROLOGICAL SOCIETY

Sunnybrook Hospital, Toronto. June 16, 17 and 18

Secretary: DR. ALLAN WALTERS, Medical Arts Bldg., Toronto.

CANADIAN PSYCHIATRIC ASSOCIATION

Royal York Hotel, Toronto. June 18.
Secretary: DR. C. A. ROBERTS, Jackson Bldg., Ottawa.

CANADIAN UROLOGICAL ASSOCIATION

Royal York Hotel, Toronto. June 20 and 21.
Secretary: DR. DAVID SWARTZ, Medical Arts Bldg., Winnipeg.

CANADIAN ANÆSTHETISTS' SOCIETY

Banting Institute, Toronto. June 20, 21 and 22.
Secretary: DR. R. A. GORDON, Medical Arts Bldg., Toronto.

CANADIAN ACADEMY OF ALLERGY

Royal York Hotel, Toronto. June 21.
Secretary: DR. T. H. AARON, 502 McLeod Bldg., Edmonton.

COLLEGE OF GENERAL PRACTICE OF CANADA

Royal York Hotel, Toronto. June 24.
Executive Director: DR. W. V. JOHNSTON, 176 St. George St., Toronto.

CANADIAN MEDICAL PROTECTIVE ASSOCIATION

Royal York Hotel, Toronto. June 22.
Secretary: DR. T. L. FISHER, 180 Metcalfe St., Ottawa.

CANADIAN ASSOCIATION OF PATHOLOGISTS

Royal York Hotel, Toronto. June 24 and 25.
Secretary: DR. D. W. PENNER, Winnipeg General Hospital, Winnipeg.

CANADIAN DERMATOLOGICAL ASSOCIATION

Hotel Sheraton-Brock, Niagara Falls. June 24 and 25
Secretary: DR. R. C. SMITH, Medical Arts Bldg., Toronto.

The Council of the Royal College of Physicians and Surgeons of Canada will meet in the Royal York Hotel, Toronto, on Sunday, June 19.

The Council of the Canadian Association of Radiologists will meet in the Royal York Hotel, Toronto, on the evening of Tuesday, June 21.

The Registrars of provincial medical licensing authorities will meet at 2.00 p.m. Wednesday, June 22, at 174 St. George St., Toronto.

ABSTRACTS *from current literature*

MEDICINE

Extraprostatic Factors in Urinary Retention.

TALBOT, H. S.: NEW ENGLAND J. MED., 251: 420, 1954.

Any disorder of micturition, even when an obstruction is obvious, should be carefully evaluated to be sure another pathological process is not present. Cystometry, cystography and frequent checking of the amount of residual urine are simple, safe and inexpensive procedures which may give information of great value in the study of micturitional dysfunction. Prostatic enlargement, or other type of bladder neck obstruction, may be accompanied by pre-existing stricture of the distal urethra, by decompensation of the detrusor muscle of the bladder or structural alterations in the bladder wall as a consequence of long-continued urinary obstruction. If the complete picture is known, the patient can be aided much more expeditiously and careful, conservative management can be instituted following operation, with particular attention to habit training.

Irreversible changes which may occur in the bladder wall as a result of long-standing obstruction may necessitate a partial cystectomy, with removal of the redundant part of the bladder wall. NORMAN S. SKINNER

Postoperative Wound Infections Due to Staphylococcus Aureus.

HOWE, C. W.: NEW ENGLAND J. MED., 251: 411, 1954.

The incidence of penicillin-resistant strains of *Staph. aureus* among hospital patients and personnel has increased markedly since the introduction of penicillin. Careful analysis of the records of the Massachusetts Memorial Hospitals over the past five years has shown that postoperative infection of clean surgical incisions has increased in step-like fashion. Study of the flora of these infected operative sites has demonstrated the importance of penicillin-resistant *Staph. aureus* as the etiological agent.

Routine prophylactic systemic antibiotic therapy is probably contraindicated in clean surgery; it should be reserved for cases in which infection subsequently occurs. Surgeons and nurses should wear masks and gloves during contact with contaminated dressings in order to prevent the development of a carrier state through the harbouring of organisms in their nasopharynx. A tendency towards carelessness in aseptic techniques, which has crept in with the advent of the era of antibiotics, must be carefully avoided.

NORMAN S. SKINNER

Control of the Complications of Diabetes: Hyperglycæmia and Glycosuria, Endogenous and Exogenous Insulin.

MOSENTHAL, H. O.: AM. J. M. SC., 227: 134, 1954.

The role of the liver in diabetes is more rationally conceived as lack of ability to assimilate and retain glucose as glycogen and fat, rather than as overproduction of glucose. Before insulin was available by injection, diabetics did not live very long, the majority of deaths being due to coma or infection which resulted from a persistent hyperglycæmia, glycosuria, polyuria and desiccation. Since the introduction of insulin, diabetics live much longer and coma has virtually disappeared as a cause of death. The development of nephritis, coronary thrombosis, retinitis and arteriosclerosis appeared

Canad. M. A. J.
Mar. 15, 1955, vol. 72

almost inevitable after 25 years of diabetes. According to Warren and LeCompte, the deposit of glycogen in the kidneys, heart, retina, and arteries, resulting from persistent hyperglycæmia and not always reversible, is the cause of such degenerative changes.

Insulin, administered by injection, is not the complete remedy for diabetes, because the greater part of the injected insulin acts in the extrahepatic tissues and results in the deposit of glycogen in them. In addition to an insulin with prolonged action, a diet containing no free sugar and a regular amount of slowly absorbable sugar (starches and, to a lesser extent, proteins), so as to adjust itself to the limited amount of insulin harboured in the liver and to prevent an inordinate postprandial rise of blood sugar, would appear to be the answer. The "free diet" plan, though it prevents death from coma and malnutrition, does not meet the demands of the present, well-founded belief regarding the cause of diabetic involvement of the kidneys, retinæ, heart, pancreas, arteries and possibly other structures.

S. J. SHANE

SURGERY

Treated Compared with Untreated Breast Cancer.

KEYES, E. L., ORRAHOOD, M. D. AND BLUMENTHAL, H. T.: A. M. A. ARCH. SURG., 68: 820, 1954.

A series of 100 cases of carcinoma of the breast operated upon by Fischel between 1928 and 1944 were compared with Daland's 100 untreated cases. The average survival period was 6 years, 1 month, compared with 3 years, 5 months in the untreated cases. Ten of these cases survived 10 years—twice as many as in Daland's series. The ages of the patients are given and their fate is discussed both from the date of the onset of the tumour and the date of the operation. If Fischel's series was made to include the 14 who refused operation during the period, the average survival time from onset was 5 years, 8 months, and the 10-year survival rate was 19% instead of 21%, compared to 5% in Daland's series. "Borderline cancer" was excluded from Fischel's series, as suggested by McKinnon.

It is concluded that radical mastectomy usually prolongs the life of patients with breast cancer but fails to cure most of them. If the cancer has spread in the breast to the stage of skin dimpling or nipple retraction or ulceration or skin metastases, it is doubtful whether the operation prolongs life. BURNS PLEWES

Results of Surgical Treatment of Carcinoma of the Œsophagus and Gastric Cardia.

CHAUNCEY, L. R.: A. M. A. ARCH. SURG., 68: 872, 1954.

The end results of treatment of 35 cases of carcinoma of the œsophagus and cardia are found to be poor indeed, but a satisfactory degree of palliation is often achieved. Though the original weight is seldom regained, postoperative weight levels are maintained and the patients live comfortably for a short time. There is little else to offer, for gastrostomy or jejunostomy gives no benefit, and the use of plastic tube grafts or anterior long jejunal detours has not yet been evaluated. Roentgen ray treatment apparently gives an average of eight months' palliation in most cases of œsophageal cancer.

Of 54 patients, 35 were considered operable and 28 underwent resection. Thus half the total patients survived a resection and were followed up; 8 are still living, for 56, 53, 41 and 33 months and less. Those with carcinoma at or above the arch of aorta were the most disappointing group. BURNS PLEWES

A Clinical Study of Two Hundred and One Cases of Regional (Segmental) Colitis.

NEUMAN, H. W., BARGEN, J. A. AND JUDD, E. S., JR.: SURG., GYNEC. AND OBST., 99: 563, 1954.

The records in 201 cases of regional (segmental) colitis seen at the Mayo Clinic between 1924 and 1950 were analysed. The disease is commonest in the third decade of life, and members of the Jewish race are particularly affected. The symptoms include diarrhœa, loss of weight, abdominal pain and fever. Common findings are abdominal tenderness and pallor of skin and mucous membranes. The commonest laboratory finding is hypochromic microcytic anæmia. In most cases both the right and the left sides of the colon were affected; malignant change did not occur. This disorder constitutes 4 to 10% of all cases of chronic ulcerative colitis, and the cause is unknown. There is a high incidence of perirectal and perianal suppuration and of polypoid change in the mucosa.

Medical management gives disappointing results, but surgical treatment is shown to be associated with more recurrence than has been thought. The incidence of recurrence appears to be about the same after short-circuiting operations and after resection. S.G.

OBSTETRICS AND GYNÆCOLOGY

Rheumatic Heart Disease in Pregnancy: The Remote Prognosis in Patients with "Functionally Severe" Disease.

GORENBERG, H. AND CHESLEY, L. C.: AM. J. OBST. & GYNEC., 68: 1151, 1954.

With proper care practically every pregnancy encountered in a patient with rheumatic heart disease can be brought to a successful termination. A follow-up study of patients with "severe" rheumatic heart disease is reported. An analysis of 133 women examined 8½ to 21 years after delivery forces the conclusion that childbearing does not accelerate the rheumatic process even in women with advanced disease. Analysis of samples of smaller sub-groups of increased severity consistentiy yielded the same conclusion.

Despite the hazards of the pregnancies themselves, one or more pregnancies after recognition of advanced heart disease did not increase the annual death rate.

In short, longevity even in patients with severe rheumatic heart disease is not adversely affected by childbearing. ROSS MITCHELL

Prognosis in Cancer of the Uterine Cervix Based on the Vaginal Smear Before Treatment.

GRAHAM, J. B., GRAHAM, R. M. AND LIU, W.: SURG., GYNEC. & OBST., 99: 555, 1954.

In a series of 136 patients treated radiologically and 103 treated by operation for cancer of the cervix, the value of the SR (Sensitization Response) has been analyzed. The SR consists in a change in cells in the vaginal smear; the affected cells have a frilly vacuolated but denser cytoplasm and stain a deep lavender with Papanicolaou's stain. From the authors' analysis it appears that the sensitization response is more marked (in over 10% of cells) in cases in which the outlook for radiotherapy is good and the outlook for operation bad. When the SR is less marked (less than 10% of all non-malignant epithelial cells seen and counted) the outlook for operation is better than that for radiotherapy. The authors are convinced that the SR is a useful prognostic index, and urge the more widespread use of the technique.

Puerperal Hemiplegia.

STEVENS, H.: NEUROLOGY, 4: 723, 1954.

A commonly unrecognized syndrome, erroneously described by some authors as rare and fatal, is the sudden onset of headache, convulsions, hemiplegia and coma in a young and healthy woman several hours to several weeks after delivery. Eight cases are reported, in all of which recovery took place. The cause is considered to be cerebral venous thrombosis. A previously undescribed feature is fluctuating hypertension, which may further contribute to an incorrect diagnosis of postpartum eclampsia.

S.G.

PÆDIATRICS

The Psychological Approach to Children's Eye Problems.

KRIMSKY, E.: POSTGRAD. MED., 15: 459, 1954.

This author maintains that one should learn to think of the eye not solely as an isolated organ, or as an appendage of the brain, but also as an external manifestation of possible disturbed psychological responses. The physician can easily discern abnormalities of the eye with the ordinary flashlight. Naturally, he must not startle the child with an abrupt approach with the light. It is best to make a game of the procedure and thus gain the child's co-operation. Thus, he can mark the normality or abnormality of the eyes and can first of all rule out such things as retrolental fibroplasia, cataract, amaurotic family idiocy, or glioma. If he assures the parents that the child will "outgrow the condition," he must base his statement on careful examination and evaluation.

A detailed account of some psychological upsets relating to the eye is presented. Hysterical blindness in the child is not uncommon. Here the child cannot see the blackboard or even the largest letter on the vision chart. Inconsistent with this is the fact that he has no trouble in walking. The physician gains his confidence by assuring him repeatedly that "I am going to make you see." At first the child will not believe him, but kindness and persistence will win him over. Then he places the child in front of the chart and juggles "lenses" in front of his eyes. At first there will be a blank response, then a state of confusion, and finally the child will be able to read the largest letters. The "lenses" are pieces of ordinary window glass. The child is finally able to read the whole chart—the examination has turned into a game for him. Now, of course, it is necessary to discover the cause of the psychological block, and treatment is by suggestion through persuasion. The cause may be a family relationship or some unhappy relationship in the school, or the child may have been shocked to learn that a playmate has become blind.

Parents make the mistake, in some instances, of attempting to make a child, who has poor vision in one eye and normal in the other, wear glasses with the idea of improving the poor eye. They must understand that sight often remains stationary and no amount of nagging the child will improve his sight. Many children resent being "boxed in" by glasses when they know that their total eyesight is not being increased. Growing boys and girls, either with pronounced near- or far-sightedness, even though they know that their eyesight is improved by glasses, resent them and refuse to wear them. There is nothing much one can do with these children since their vanity far outweighs any desire for clear vision. They do, however, develop compensations which allow them to get along.

The numerous superstitions about eyesight which have come with television are unfounded. If the child develops a twitching or tremor of the eyelid this is more likely to be the sign of a psychological breakdown than of too much television. Television, in fact, has increased the desire for glasses, and thus sharper vision.

Of course, none of these factors should be discussed in the presence of the child—it isn't good medicine since the reaction of the parent may serve to make matters worse. Too often, psychological eye problems in children arise from environmental shock emanating from the parent, doctor or teacher, another child, or a relative.

ISABEL M. LAUDER

Congenital Paralytic Ileus in a Premature Baby as a Complication of Hexamethonium Bromide Therapy for Toxæmia of Pregnancy.

HALLUM, J. L. AND HATCHUEL, W. L. F.: ARCH. DIS. CHILDHOOD, 29: 354, 1954.

The authors report a case of paralytic ileus in a premature baby after the mother had been treated during pregnancy with hexamethonium bromide. The patient was treated in hospital for pre-eclampsia, and given 50 mgm. of hexamethonium bromide subcutaneously every six hours; after 15 days, a Cæsarean section was performed. The baby failed to pass an appreciable quantity of meconium until a bowel wash-out was done on the fifth day. Peristalsis was diminished and there was gaseous distension of the entire gut, lasting from shortly after birth until the third week of life. The character of the stools changed only during the second week and normal size and consistency were assumed only at the end of the third week.

The authors considered that in their case the continued administration of hexamethonium bromide to the mother to the time of the Cæsarean section had resulted in a high fetal blood level of the drug, and that this in turn had caused lethargy and paralytic ileus, the symptoms of which had abated as the drug was excreted from the baby's bowel. Excretion of the drug is probably by glomerular filtration; the prolonged symptoms in this case confirmed this idea since glomerular filtration in premature babies is very poor. The authors also point out that œdema neonatorum, which occurred in this baby, would also support this hypothesis.

W. F. T. TATLOW

Cerebral Palsy Research and the Preschool Years.

GESELL, A.: POSTGRAD. MED., 15: 104, 1954.

The author, long a pioneer in the study of child development, makes a plea for education of the profession and the public in the need for more research in this special field. He points out that the public visualizes this handicapped group as attending special schools with special equipment. While this is indeed true, it seems that little or no cognizance has been taken of the preschool years of these children. His thesis is that the early years are supremely significant for research, and for programmes of care and education. His reasons are: (1) Cerebral palsy (and injury) originate mainly in prenatal and circumnatal factors. (2) The genesis and evolution of symptoms can be investigated most advantageously in infancy. (3) Early and cumulative diagnosis facilitates all supervisory and guidance measures and helps the family toward an optimal, realistic acceptance of the child's handicap. Every infant is faced with achieving an allotted measure of maturity. We must know something of the growth potentials of these handicapped children if we are to help them.

Gesell points out that cerebral injury need not be so massive as to leave the child with palsy. Minimal injuries play a part in distorting personality patterns too. More is learned daily about this little-understood factor. This group consists of those infants who make a slow or delayed recovery, or in whom behaviour deviations persist, apparently due to injury. The risk of permanent

Canad. M. A. J.
Mar. 15, 1955, vol. 72

residuals is least in children of superior endowment and high growth potentials. An undetermined fraction of reading disabilities can be ascribed to obscure minimal injuries which damage perceptual organization.

The author insists that much more can and should be done for these children, especially in their preschool years, which are of critical importance in charting the course for later years. ISABEL M. LAUDER

THERAPEUTICS

Treatment of Hypertension.

DENNIS, E. *et al.*: POSTGRAD. MED., 16: 300, 1954.

Ninety patients were studied; 24 with hypertension of varying degree of severity were treated with Alseroxylon (Rauwiloid) alone for one year or more. The response was just as great after 12 months of continuous treatment as it had been after the initial six months of therapy.

Of 66 patients with varying degrees of hypertension, who were treated with combined Alseroxylon (Rauwiloid) and hexamethonium for at least one year, 89% maintained a reduction of 20 mm. Hg in their blood pressure during the six to 12 month period of treatment. About half the patients became normotensive.

It was concluded that the reduction of blood pressure following combined Alseroxylon (Rauwiloid) and hexamethonium treatment was greater in degree and more stable than with hexamethonium alone. The addition of Alseroxylon (Rauwiloid) to hexamethonium therapy decreased the incidence and severity of side reactions. B. L. FRANK

Chlorpromazine—A Major Advance in Psychiatric Treatment.

KINROSS-WRIGHT, V.: POSTGRAD. MED., 16: 297, 1954.

For long psychiatrists have searched for a simple agent with which to treat mental illness, one effective without producing narcosis or coma and at the same time increasing the patient's capacity to respond to psychotherapy. Chlorpromazine, a derivative of phenothiazine which appears to fulfil these requirements, was recently discovered. Chlorpromazine influences both divisions of the autonomic nervous system. It produces temporary hypotension with associated tachycardia. By direct action on the medullary centres it suppresses nausea and vomiting. The way in which it alters behaviour is not quite understood but its effects are probably mediated via the diencephalic region of the brain. Quite small doses produce sleepiness and reduction of motor activity. However, even with ten times the average therapeutic dose the sleepiness does not approach coma. Patients may be aroused easily and will converse rationally.

Chlorpromazine was tried in most types of mental disorder with varying degrees of success. Psychotic patients received 50 to 100 mgm. by deep intramuscular injection four times daily. This dose was increased by an additional 100 to 200 mgm. in a 24 hour period every other day. Intramuscular injection was often painful and, as soon as the patient calmed down and slept most of the day, oral medication was gradually substituted. The maximum daily amount of chlorpromazine was determined by the nature of the illness and the individual response. As much as 2,000 mgm. a day was given, though the average requirement was about 400 to 600 mgm. per day. In the average case the maximum dosage was reached in about seven days, maintained for another week and then progressively decreased. The maintenance level of 100 to 200 mgm. a day was continued for weeks or months. In the majority of patients chlorpromazine was discontinued within two months.

Cases of minor mental illness such as anxiety neuroses, tension states, hysteria, psychosomatic illnesses, migraine, tics and general nervousness were treated with an average dose of 25 mgm. three times a day. While the drug was helpful in treating many of these patients, it rarely cured them. However, it did give the patient a feeling of well-being, improved his physical status and often increased his acceptance of psychotherapy. Hypertensive patients in particular benefited from the relaxation of tension and reduction of blood pressure to normal levels.

No dangerous side-effects were noted. (A case of agranulocytosis following the use of chlorpromazine in a woman of 69 was reported in *Brit. M. J.*, 2: 358, 1954.) Allergic manifestations such as dermatitis were not uncommon. Dryness of the mucous membranes, nasal stuffiness and slight blurring of vision were common minor effects. A few patients had a transient high spiking temperature during the first few days of treatment. In a few patients, parkinsonism developed unexpectedly, but receded when chlorpromazine was discontinued. B. L. FRANK

INDUSTRIAL MEDICINE

Health Maintenance and Accident Prevention in Retail Stores.

INDUST. MED., 23: 468, 1954.

The recent increase in accident rates in retail stores has contributed largely to the ever-increasing workmen's compensation costs with which management is faced. According to insurance companies this rate is still on the rise, except where planned and thorough loss prevention programmes have been instituted.

In this article, which is a report to management, the situation as regards accidents in stores and costs involved is presented, together with information regarding the value of successful accident reduction programmes. One New York store, among several which have adopted programmes combining health maintenance with safety education, lowered its measurable accident costs by 40% in about 18 months.

The relation which can exist between the medical department and safety is discussed with special reference to the following:

1. *Pre-placement medical examination of the new employee.* The object of this is to keep employees from being assigned to work that presents special accident or health risks to the individuals concerned. The responsibilities of the doctor will vary according to the policy of the store. It is recommended that the store doctor be given a systematic education in the jobs and the working conditions.

2. *Periodic examination of each employee and post-absence check-up,* also *health counseling.* Of importance is the accident hazard represented by people suffering the beginnings of illness, or from worry or emotional disturbance. A good medical department can render useful service to this large category of people. In this connection, the nature of the personnel is most important; they must be courteous, understanding, and sympathetic within reason.

3. *Maintenance of careful records and analysis of injuries and illnesses reported.* These often point out an uncorrected hazard or a situation needing attention.

Reference is made also to the relation between a good medical programme for a store and the support

received from management. The role of the safety director is outlined together with that of doctor, nurse and secretary.

MARGARET H. WILTON

Carbon Tetrachloride Poisoning—A Review.

HARDIN, B. L. JR.: INDUST. MED., 23: 93, 1954.

Although carbon tetrachloride has been abandoned in medicine, the extensive experimental work done in connection with its use has enabled the medical profession to give advice regarding its role in industry. This article presents a history of the subject gleaned from an extensive review of available literature.

The author first presents information on the chemistry of carbon tetrachloride, its use as an anæsthetic and analgesic, as a shampoo, as an anthelmintic, and in industry. Its use as an anæsthetic agent and as an analgesic was of short duration owing to the realization that it was more toxic and less effective than chloroform. The opinions of physicians who experimented with it between 1865 and 1877 were hardly favourable. Its use, early in this century, as a dry shampoo was also short-lived, owing to evidence of its danger. As a vermifuge for the hookworm it was in the medical limelight for a few years, but occasionally illness and even death resulted from its use; owing to its toxic properties it has been superseded as an anthelmintic by the appreciably less toxic tetrachlorethylene. Today its widespread use in industry as solvent, degreaser, fire extinguisher, dry cleaner, and ingredient in the manufacture of Freons has resulted in increased research in the problem of human susceptibility to poisoning from it.

After tabulating symptoms, signs and significant autopsy findings obtained by analyzing 77 selected cases of subacute poisoning found in the American and English literature between 1939 and 1953, the author concludes that "treatment for any form of carbon tetrachloride poisoning consists of nothing specific; there is no drug that antagonizes carbon tetrachloride or alleviates the damage done to the kidney or the liver. Treatment is really helping nature to tide the patient over until the regenerative power of the affected hepatic and renal cells builds them back to normal again."

MARGARET H. WILTON

Employment Problems of the Cardiac.

SCOTT, H. J.: INDUST. MED., 23: 449, 1954.

"To assist those afflicted with cardiac disease in their efforts to obtain employment in public and private industry" is presented in this article as the essential objective of a "cardiac in industry" committee. The author, a lawyer and member of the Cardiac in Industry Committee of the Los Angeles County Heart Association, reviews the development of the law in California in reference to so-called heart cases in industry and shows how the present legal situation has created a serious problem.

Under early workmen's compensation law the two essential requirements for liability are that the injury or disease arise out of the employment, and that it occur in the course of employment. When considering a claim for heart disease, until 1946 the courts held that the causation requirement was met only by showing that the injury involved a violent exertion and extraordinary strain over and above the employee's usual duties. In 1946, solely by judicial interpretation, the requirement that the employment should have caused the heart injury was eliminated. Cases are decided now purely on the basis of the onset of acute symptoms while the man is working.

The author shows how this change has affected the employer and has nullified efforts to encourage industry to employ persons handicapped by heart disease. In his opinion the entire blame cannot be assigned solely to the Industrial Accident Commission, the courts, the attorneys, or the claimant himself. He feels that the medical reports are frequently not adequate.

In spite of the present difficulties the Committee are continuing their efforts to promote their objective. A so-called Work Classification Unit is now being put into operation. It is necessary, however, if the employ-the-handicapped programmes are to have any chance of success, that the employer be given some protection.

MARGARET H. WILTON

PUBLIC HEALTH

Tuberculosis in Ontario.

BRINK, G. C.: CANAD. J. PUB. HEALTH, 45: 195, 1954.

Tuberculosis is still a major public health challenge in Ontario, although there has been a marked decline in mortality during the last quarter century and more especially in the last seven years. The number of new cases admitted to sanatoria annually during the last ten years shows no significant change, but there has been an increase of 21 to 27% in population over the same period and therefore a decrease in new admissions from 54 per 100,000 population in 1943 to 47 in 1952. The percentage of reactors to tuberculin in all age groups has decreased: in 1923 58% of high school students tested were reactors and today the percentage has dropped to below 10%. In 1951 in a review of a cross-section of discharges from sanatoria in Ontario it was found that less than 17% were readmitted within five years of their original discharge and only 21% within 10 years. These figures refer to pre-antibiotic days and the present reactivation rate may be somewhat less. One of the most striking changes has been that tuberculosis is becoming increasingly a disease of people over 50 years of age, especially males.

The first two years after arrival in Canada is the time when active disease is most likely to develop in an immigrant, but there has been a decline in the incidence of tuberculosis amongst immigrants since 1947 and 1948.

The medical practitioner has been the most important person in the finding of tuberculosis. In a recent survey it was found 18% of patients entering sanatoria had been diagnosed by the private physician in his office, and that the physician was indirectly involved in the diagnosis of another 40%. Seventy-nine per cent of all general hospitals in the province reported a coverage of 70% and over of patients routinely radiographed in a case-finding project in the last quarter of 1953. The cost of tuberculosis in Ontario, excluding loss of wages and purchasing power, has been estimated to be nearly twelve million dollars annually; hence there is no basis for complacency. The challenge is to bring to light all undiagnosed cases of tuberculosis; and every possible approach must be explored to the maximum with the co-operation of official and voluntary agencies, the medical and nursing professions, and the general public itself.

W. F. T. TATLOW

Canad. M. A. J.
Mar. 15, 1955, vol. 72

FORTHCOMING MEETINGS

CANADA

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS, Winnipeg, Manitoba. (Dr. P. H. T. Thorlakson, Chairman.) April 25-26, 1955.

CANADIAN HOSPITAL ASSOCIATION, Biennial Meeting, Ottawa, Ont. (Executive Director: Dr. W. D. Piercey, 280 Bloor Street West, Toronto 5, Ont.) May 9-11, 1955.

COMMONWEALTH MEDICAL CONFERENCE OF THE BRITISH MEDICAL ASSOCIATION, Toronto, Ontario. (Dr. A. D. Kelly, Canadian Medical Association, 244 St. George Street, Toronto 5.) June 14-16, 1955.

BRITISH MEDICAL ASSOCIATION, CANADIAN MEDICAL ASSOCIATION, ONTARIO MEDICAL ASSOCIATION, Conjoint Meeting, Toronto, Ont. (Dr. A. D. Kelly, General Secretary, Canadian Medical Association, 244 St. George Street, Toronto 5, Ont.) June 17-24, 1955. (Scientific Sessions June 20-24.)

CANADIAN ACADEMY OF ALLERGY, Annual Meeting, Royal York Hotel, Toronto, Ont. (Dr. P. A. Ryan, Acting Secretary, 229 St. Clair Avenue West, Toronto 7, Ont.) June 21, 1955.

CANADIAN PUBLIC HEALTH ASSOCIATION AND ALBERTA PUBLIC HEALTH ASSOCIATION, Conjoint Meeting, Edmonton, Alta. (Dr. William Mosley, Honorary Secretary, 150 College Street, Toronto 5, Ont.) September 6-8, 1955.

UNITED STATES

AERO MEDICAL ASSOCIATION, Twenty-sixth Annual Meeting, Hotel Statler, Washington, D.C. (Dr. O. O. Benson, Jr., Brigadier General, U.S.A., President.) March 21-23, 1955.

AMERICAN ACADEMY OF GENERAL PRACTICE—7th Annual Scientific Assembly, Los Angeles. (Mr. Mac F. Cahal, Broadway at Thirty-fourth, Kansas City 11, Missouri.) March 28-31, 1955.

AMERICAN ACADEMY OF PEDIATRICS, Spring Session, Sheraton-Cadillac Hotel, Detroit, Michigan. (Dr. E. H. Christopherson, Executive Secretary, 610 Church Street, Evanston, Illinois.) April 4-7, 1955.

SECOND MICROCIRCULATORY CONFERENCE, Philadelphia, Pa. (Dr. G. P. Fulton, Chairman, Boston University, College of Liberal Arts, 725 Commonwealth Avenue, Boston 15, Mass.) April 5, 1955.

AMERICAN ASSOCIATION OF ANATOMISTS, Philadelphia. (Dr. N. L. Hoerr, Secretary, 2109 Adelbert Road, Cleveland, Ohio.) April 6-8, 1955.

AMERICAN DERMATOLOGICAL ASSOCIATION, Belleair, Florida. April 17-21, 1955.

AMERICAN RADIUM SOCIETY, Annual Meeting, Shoreham Hotel, Washington, D.C. (Dr. R. E. Tricke, Secretary, Mayo Clinic, Rochester, Minn.) April 21-23, 1955.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Shoreham Hotel, Washington, D.C. (Dr. E. P. Pendergrass, Secretary-General, 3400 Spruce Street, Philadelphia 4, Pa.) April 24-29, 1955.

AMERICAN COLLEGE OF PHYSICIANS, Philadelphia, Pa. (Mr. E. R. Loveland, Executive Secretary, 4200 Pine Street, Philadelphia 4, Pa.) April 25-29, 1955.

AMERICAN GOITER ASSOCIATION, 1955 MEETING, Skirvin Hotel, Oklahoma City, Oklahoma. (Dr. J. C. McClintock, Secretary.) April 28-30, 1955.

AMERICAN PSYCHOSOMATIC SOCIETY, Annual Meeting, Atlantic City, N.J. May 4-5, 1955.

AMERICAN UROLOGICAL ASSOCIATION, Biltmore Hotel, Los Angeles, California. (Dr. C. H. de T. Shivers, Secretary, 121 S. Illinois Ave., Atlantic City, N.J.) May 16-19, 1955.

EIGHTH ANNUAL INDUSTRIAL MICROBIOLOGY INSTITUTE, West Lafayette, Indiana. (Dr. C. L. Porter, Director of the Institute, Department of Biological Sciences, Purdue University, West Lafayette, Indiana.) June 5-11, 1955.

AMERICAN MEDICAL ASSOCIATION, 1955 Annual Meeting, Atlantic City, N.J. (Dr. George F. Lull, Secretary, 535 North Dearborn Street, Chicago 10, Ill.) June 6-10, 1955.

OTHER COUNTRIES

SIXTH LATIN AMERICAN NEURO-SURGICAL CONGRESS AND SECOND LATIN AMERICAN ELECTROENCEPHALOGRAPHICAL CONGRESS, Montevideo, Uruguay. (Dr. R. Arana-Iniguez, Convencion 1287, Montevideo, and Dr. P. Pinto Pupo, San Pablo, Brazil.) March 21-24, 1955.

JAPAN MEDICAL CONGRESS, Kyoto, Japan. (Dr. M. Goto, Secretary General, University Hospital, Medical Faculty of Kyoto University, Kyoto, Japan.) April 1-5, 1955.

TENTH CONGRESS OF THE INTERNATIONAL UROLOGICAL SOCIETY, Athens. (Prof. Z. Kairis, rue Voukourestiou 25, Athens.) April 10-18, 1955.

MIDDLE EAST MEDICAL ASSEMBLY OF THE AMERICAN UNIVERSITY OF BEIRUT, American University campus, Beirut, Lebanon. (Dr. John L. Wilson, Professor of Surgery, Chairman, Committee for the Fifth Middle East Medical Assembly.) April 22-24, 1955.

WORLD HEALTH ORGANIZATION—8th General Assembly, Mexico City. (World Health Organization, Palais des Nations, Geneva, Switzerland.) May 10, 1955.

FIFTEENTH CONGRESS OF FRENCH-SPEAKING PÆDIATRICIANS, Marseilles, France. (Dr. Réné Bernard, Clinique Médicale Infantile, Hôpital de la Conception, Marseilles.) May 23-25, 1955.

INTERNATIONAL COLLEGE OF SURGEONS—20th Anniversary Meeting, Geneva, Switzerland. (Dr. Max Thorek, 850 West Irving Park Road, Chicago 13, Ill.) May 23-26, 1955.

SEVENTH INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Lausanne, Switzerland. (Prof. Hauduroy, 19 avenue César-Roux, Lausanne.) May 26-31, 1955.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland. (Capt. J. E. Stone, Hon. Secretary, International Hospital Federation, 10 Old Jewry, London, E.C.2, England.) May 29-June 3, 1955.

EUROPEAN CONGRESS ON RHEUMATISM, Scheveningen, The Hague, Netherlands. (Dr. H. van Swaay, Secretary, Pieter Bothstraat 12, The Hague, Netherlands.) June 13-17, 1955.

FIFTH CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Stockholm, Sweden. (Dr. J. M. Lemoine, 187 boulevard Saint-Germain, Paris 7e.) June 18-19, 1955.

FOURTH COMMONWEALTH HEALTH AND TUBERCULOSIS CONFERENCE, Royal Festival Hall, London, England. (Secretary-General, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1, England.) June 21-25, 1955.

SECOND CONGRESS OF THE INTERNATIONAL DIABETES FEDERATION, Cambridge, England. (Organizing Secretary, Mr. J. G. L. Jackson, Congress Office, 152 Harley Street, London, W. 1, England.) July 4-8, 1955.

NEWS ITEMS

MANITOBA

A 65-bed hospital was opened on February 3 at Selkirk by Ernest Setter, chairman of the hospital board. It replaces the old building which served the community for 49 years. A two-storey residence for nurses has also been built beside the hospital. Both buildings are of low, modern design.

Dr. S. S. Peikoff has been appointed president of the medical staff of St. Boniface Hospital. Others elected were Dr. H. Guyot, first vice-president, Dr. Paul Green, second vice-president, Dr. R. T. James, secretary, Dr. L. R. Rabson and Dr. J. Downey members.

Thirty Winnipeg doctors left for Regina on February 3 to attend a two-day clinical meeting of the prairie region, American College of Physicians. In charge was Dr. C. H. A. Walton, governor of this region. Among the speakers were Dr. Louis Cherniak, Dr. A. B. Houston and Dr. F. A. L. Mathewson.

Dr. S. Vaisrub has been appointed editor of the *Manitoba Medical Review*. ROSS MITCHELL

ONTARIO

A new prison hospital, the first of its kind in Canada, has been opened at Guelph Reformatory, for the treatment of the prison population of Ontario. The hospital, a two-storey building, provides accommodation for 50 patients and has modern x-ray and laboratory equipment, including an electroencephalograph. Dr. F. Van Nostrand will supervise the institution. A psychiatric clinic will be set up, to which patients from other reform institutions will be referred.

A new project of the Women's Auxiliary, Mount Sinai Hospital, Toronto, is a health education lecture series given by members of the medical staff. Topics of lectures include The Out-Patient Department, How it Operates; Diet Fads; What is Hospital Research; Three Stages in Every Woman's Life; and Successful Marriage and Parenthood.

In Metropolitan Toronto (the city and suburbs) 27,527 babies were born in 1954; that is, more than 75 babies a day were delivered. Infant mortality dropped to a new low of 22 deaths per 1,000 live births. Deaths from all causes totalled 8,458.

St. Michael's Hospital, Toronto, established sixty-two years ago, is making its first public appeal for financial help. The sum to be raised is $5,105,000.

Dr. A. Earl Walker, neurosurgeon-in-chief, Johns Hopkins Hospital, and Professor of Neurosurgery, Johns Hopkins University, recently addressed the Toronto Academy of Medicine on "Current Concepts of the Physiology and Therapy of Epilepsy." He pointed out that all the present clinical types were described a long time ago, and showed slides of various brain lesions responsible for epilepsy. His interest had been stimulated by the recurrence of seizures after the removal of a spike focus surgically, and even after hemispherectomy, also by the fact that some patients with focal seizures had an associated generalized cerebral dysrhythmia. The conclusion reached was that the cerebral cortex is not the most important source of focal seizures.

He described experimental work with a special electrode holder with 44 needles for recording cortical and subcortical leads simultaneously from the brain of a macaque monkey. The position of the subcortical electrodes was checked pathologically at the conclusion of the experiment. The brain was stimulated either by an electrical stimulus of 5 volts for 5 seconds at 30 cycles per second, or by inserting a deposit of penicillin which produced an adequate stimulus.

Results of the experiments showed that focal seizures can be initiated by either cortical or subcortical stimulation. Two main circuits are involved. (1) Amygdalo-hippocampal-anterior temporal region with very little effect on the cortex. The cerebellum is not involved. (2) Cortex, putamen and globus pallidum. The latter are grossly involved in cortical attacks. The cerebellum is also involved.

Therapeutic implications are that anticonvulsants should be given an adequate trial because so many structures are involved, and that an attempt must be made to remove the entire system involved when neurosurgery is used; for example, cortical focal seizures may be modified by removal of the putamen and globus pallidum. This has been done in Japan. Further research should indicate a type of surgical approach which will avoid creation of severe motor and sensory deficits.

LILLIAN A. CHASE

QUEBEC

The principal and vice-chancellor of McGill University recently announced the creation of a new department of investigative medicine, with Dr. J. S. L. Browne in charge, effective July 1, 1955. At the same time Dr. Browne will relinquish his posts of professor of medicine, chairman of the department of medicine, and director of the Royal Victoria Hospital University Clinic. The new department will offer courses and training leading to the degrees of M.Sc. and Ph.D. in the faculty of graduate studies and research. Dr. Browne, one of the most popular teachers of undergraduates and graduates, was the guest of honour at the annual dinner of the McGill Medical Undergraduates' Society on January 24.

In 1953 the Provincial Government set up a committee, consisting of Dr. Gérard LaSalle, superintendent of the University of Montreal hospital, Dr. Lucien LaRue, Quebec, superintendent of the St. Michel Archange hospital for mental patients, and Mr. Jack Latter, a Quebec businessman, to study the hospital situation in the Province. In accordance with their recommendation the Quebec government has decided to build three 1,500-bed mental hospitals at a cost of $55,000,000. These hospitals will be erected in Three Rivers, Sherbrooke and Joliette. Technical advisers on this study were Dr. Jean Grégoire and Dr. J. C. Beaudet, Quebec Deputy Health Ministers.

On January 7, the Montreal Medico-Chirurgical Society held a panel discussion on the role of drugs in treatment and their relationship to the cost of sickness. Mr. George S. Currie, C.A., was in the chair and panel members included Dr. D. Sclater Lewis and Dr. Campbell Gardner, Mr. John B. Frosst, vice-president of Charles E. Frosst and Company, and Mr. William Leslie, president of Ayerst, McKenna and Harrison Limited. Dr. Sclater Lewis emphasized that the expense of drugs was not an important factor in the cost of illness. He added that if there was over-prescribing, the fault lay equally with the drug manufacturer, the doctor and the patient. Dr. Gardner suggested that doctors should keep up to date on medical knowledge to avoid prescribing expensive drugs when cheaper ones would do, or even ordering a drug when none is required.

Mr. Frosst emphasized that new equipment and improved methods had enabled drug houses to reduce the cost of preparations to a minimum. Mr. Leslie said that research has lowered the cost of sickness by development of new drugs. The cost of research represents about 5% of the gross sales of drugs.

Canad. M. A. J.
Mar. 15, 1955, vol. 72

The seventh annual Harold B. Cushing Memorial Lecture, sponsored by the Nu Sigma Nu fraternity at McGill, was given by Dr. Thomas Hale Ham of Western Reserve University. He outlined the new medical teaching programme at Western Reserve. This involves abandoning the highly departmentalized methods of teaching of most medical schools. Instead of the study of anatomy, physiology and biochemistry as separate subjects in the first year, organs and organ systems are studied as a whole and this is co-ordinated with the clinical and bedside teaching.

On January 19, Dr. Joseph J. Bunim, clinical director of the National Institute of Arthritic and Metabolic Diseases of the U.S. National Institutes of Health, Bethesda, speaking to the Montreal Medico-Chirurgical Society, reviewed current treatment of rheumatoid arthritis. He said that metacortandricin, a new synthetic steroid four times as potent as cortisone, had brought striking improvements to many patients suffering from rheumatoid arthritis. He stressed that it is too early to be confident of the results that this new steroid will bring. It has, however, shown considerably greater possibilities than cortisone and it is hoped the drug will be developed still further.

Like cortisone, metacortandricin was sometimes accompanied by undesirable after-effects. Two patients treated with it developed duodenal ulcers but the ulcers were healed by medication. Other patients became depressed.

Dr. James J. E. O'Neill of Philadelphia spoke recently to the McGill Sigma Xi group, emphasizing that coronary artery disease has shown signs of yielding to the efforts of the surgeons. As a surgeon he emphasized that a partially new blood supply to the vital heart muscle can be effected by surgical means, using a variety of techniques at present under experimental evaluation.

The new Montreal General Hospital will receive a cobalt bomb unit for treatment of patients with cancer. Funds for the purchase of this unit were donated by Mr. J. W. McConnell. The unit will be in operation by June 1, 1955, when the new hospital will be open. The bomb will be used principally for the treatment of deep-seated tumours where lower voltage x-ray methods are not effective.

A. H. NEUFELD

NEW BRUNSWICK

Dr. H. S. Wright has been elected Mayor of Fredericton by acclamation for a fourth term.

Dr. M. L. Jewett of Millville is reported to be recovering from a severe heart attack in the Victoria General Hospital, Fredericton.

Early in January the new $1,200,000 Carleton County Hospital in Woodstock was declared open. Speakers at the ceremony included the Lieutenant-Governor, the Hon. D. L. MacLaren; the Premier of the Province, the Hon. Hugh John Flemming; and the Hon. J. F. McInerney, M.D., the Minister of Health. The new building replaces the former Fisher Memorial Hospital.

Dr. R. L. Denton, Professor of Pædiatrics at McGill University, addressed the Saint John Medical Society on January 20 on the diagnosis and treatment of anæmia. On January 18 he gave this paper and in addition discussed modern methods of blood transfusion at Chatham and Newcastle, N.B. At Moncton on January 19 he presented a paper on the Rh factor to the Moncton Medical Society.

Dr. J. A. Melanson, Chief Medical Officer, Dr. A. M. Clarke, Assistant Chief Medical Officer, and Dr. C. R. Prosser, Director of the Mental Health Division, New Brunswick Department of Health, attended the 17th annual meeting of the Health Planning Committee of the Maritime Provinces and Newfoundland at Halifax on January 11 to 13.

The pros and cons of service versus indemnity medical care plans in Canada were reviewed by Dr. F. W. Jackson, Director of Health Servicees, Department of National Health and Welfare, Ottawa, at Fredericton on January 28. Dr. Jackson also gave an assessment of the situation in New Brunswick. He was assisted by Mr. C. L. Francis, Research Division, Department of National Health and Welfare. Dr. A. F. Van Wart, chairman of the N.B. Committee on Economics, introduced the speakers and the subject for discussion.

A. S. KIRKLAND

NEWS OF THE MEDICAL SERVICES

Canadian Armed Forces

Naval Headquarters has announced the promotion of Surgeon Lieutenant Commander P. O. Gallagher, R.C.N. (Reserve), to the rank of Surgeon Commander. Dr. Gallagher is attached to H.M.C.S. *"Cabot"*, the Reserve Division at St. John's, Newfoundland.

Surgeon Lieutenant D. A. Maciver, R.C.N., has been appointed as Principal Medical Officer to the cruiser H.M.C.S. *"Quebec"*, which is circumnavigating the continent of Africa on her current cruise. He has replaced Surgeon Lieutenant Commander R. F. Plumer, R.C.N., who was appointed for duties in the R.C.N. Infirmary, Naval Air Station, Dartmouth, N.S.

High praise was accorded the Medical Branch of the Royal Canadian Navy for its successful efforts in saving lives in the incident of the methyl alcohol poisoning aboard the aircraft carrier *"Magnificent"*. The Command Medical Officer of the Atlantic Command, Surgeon Captain F. G. W. MacHattie, directed and co-ordinated the treatment programme.

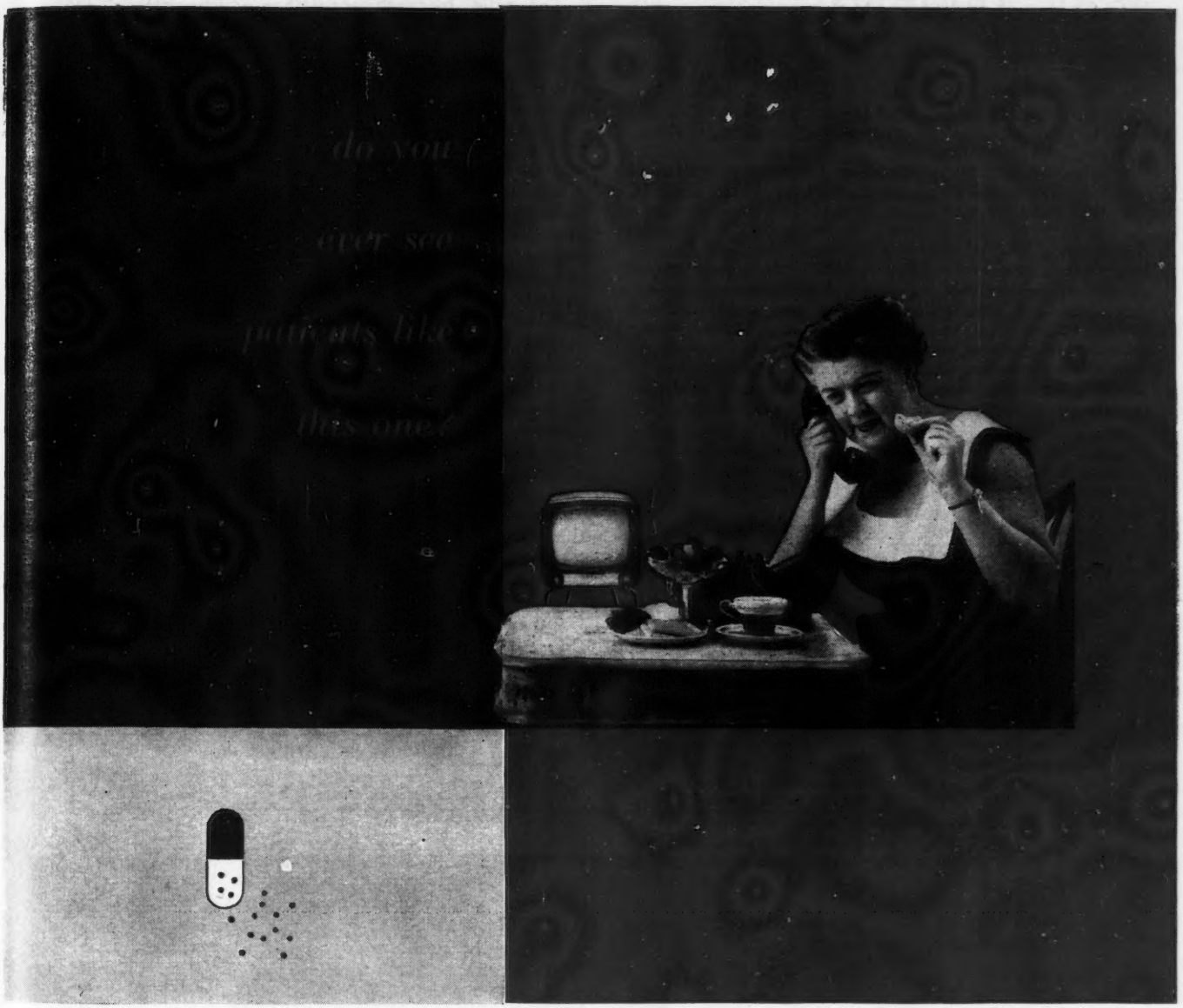
Captain N. R. T. Fink was posted to the Military Component, Canadian Delegation, Indo-China, on January 10, to assist in the medical care of Canadian personnel of the various delegations.

Wing Commander A. M. Beach, D.F.C., was promoted to the rank of Wing Commander effective January 1, 1955.

An R.C.A.F. Medical Officer attended Course No. 104, Medical Officers Indoctrination Course in Civil Defence, which was held at Arnprior, Ont., from February 28 to March 4.

Wing Commander W. J. Young, D.S.O., M.B.E., C.D., Staff D.G.M.S. (Air), visited R.C.A.F. units in 1 R.C.A.F. Air Division in Europe and the United Kingdom.

Wing Commander H. J. Bright, Staff Officer, Medical Services, R.C.A.F. Training Command, has received certification as a specialist in Aviation Medicine by the American Board of Preventive Medicine.



Grace has two grown children who now live in other cities. After years of intense activity, she is left with little to do and think about. Her days are spent with the television set and telephone, and she is usually nibbling. Her weight increases slowly, but steadily.

You can help patients of this type with 'Dexedrine Spansule' capsules. One 'Dexedrine Spansule' capsule, taken in the morning, controls appetite all day long, *between meals* as well as at mealtime . . . helping to eliminate the succession of candies, snacks, and drinks that contribute so heavily to weight gain.

Dexedrine*
dextro-amphetamine sulfate, S.K.F.

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made only by
Smith Kline & French, Montreal 9 • *the originators of sustained release oral medication*

521

* Reg. Can. T.M. Off. Patent applied for

Canad. M. A. J.
Mar. 15, 1955, vol. 72

BOOK REVIEWS

PROCEEDINGS OF THE FIRST WORLD CONFERENCE ON MEDICAL EDUCATION, held under the auspices of the World Medical Association, London, 1953.

804 pp. 60/-. Geoffrey Cumberlege: Oxford University Press, London, New York, Toronto, 1954.

Before the First World Conference on Medical Education took place in London in 1953, there was much pessimism about the outcome. After the conference, there was not only relief that the pessimism had not been justified but also rejoicing that so much good material had come out of such a diverse gathering. Indeed, the verdict was so favourable that the World Medical Association has been moved to sponsor a second conference in 1958, probably in the United States.

The Proceedings of this historic conference are now available in book form to medical educators everywhere; those connected with medical education will certainly need to refer frequently to this material, which bears the mark of the careful preparation expected from a combination of the *British Medical Journal* staff with the Oxford University Press.

All the papers given, as well as the summary reports of section proceedings, are here, together with abstracts of discussion. As usual at international meetings, remarks made in discussion vary from the inspired to the fatuous, but the proportion of the latter seems lower than usual.

The four sections of the conference were devoted to: (1) requirements for entry into medical schools; (2) aims and content of the medical curriculum; (3) techniques and methods of medical education; (4) preventive and social medicine. As a broad generalization, it may be said that the first two sections provoked the largest crop of contradictory statements, the third section the most detailed and down-to-earth results, and the fourth the most philosophical discussion.

THE WORK OF SIR ROBERT McCARRISON

Edited by H. M. Sinclair. 327 pp. $6.00. Faber and Faber Limited, London; British Book Service (Canada) Ltd., Toronto 6, 1954.

The monumental contributions made by Sir Robert McCarrison in the field of nutritional research are all too often overlooked in current publications devoted to that field. This book attempts to collect his important publications and is published on the occasion of his 75th birthday.

The brief biographical outline which prefaces the book does not do justice to a man who spent almost 35 years actively engaged in research on such diverse subjects as goitre, stone, beri-beri, and the deficiency states. The editor of this volume attempts to evaluate the work of Sir Robert McCarrison by means of a series of prologues written by different authors. These chapters offer an almost insurmountable barrier to one interested in reading the actual writing of McCarrison.

The edited publications of Sir Robert McCarrison come as a welcome relief after the confusing disjointed prologues referred to above. The skill and care of his experiments are amply matched by the lucid accounts of his work. The careful attention paid to detail and the caution observed in the drawing of conclusions might well be a standard against which a large volume of current publications could be measured.

Sir Robert McCarrison lived and worked during the first third of this century in India. His laboratory was, in essence, the great population masses of that country, and his materials were diet and nutrition. His skill in the art of careful observation, combined with an actively inquiring mind, served to elevate him to a point of pre-eminence in the field of nutritional research. His work in the field of beri-beri strengthened the hypothesis that this disease was indeed due to thiamine deficiency, in contradistinction to the infective and toxic theories then prevalent. He demonstrated, 25 years before Astwood described thiouracil, the presence of a positive goitrogenic agent in man, when he and a group of volunteers produced goitre in themselves by drinking polluted water from an area where there was a high incidence of endemic goitre.

Reading the original papers of Sir Robert McCarrison is a rewarding experience, but he deserves better treatment than is afforded him in this book.

HORMONES IN HEALTH AND DISEASE

Edited by R. L. Craig. 346 pp. illust. $6.00. The Macmillan Company, New York; The Macmillan Company of Canada Limited, Toronto, 1954.

This volume is a collection of 21 papers presented at a series of meetings of the New York Academy of Medicine by outstanding clinicians, biochemists and physiologists. The subject matter is carefully and wisely selected from the great volume of clinical and laboratory data which have become available in recent years and the contributions are of practical importance to both specialist and general practitioner.

As might be expected, hormones of the adrenal cortex and of the anterior pituitary are comprehensively dis-

cussed by E. C. Kendall and by Abraham White. Their practical application is adequately covered by C. Ragan, who emphasizes that their use requires an understanding of their mode of action not only as anti-inflammatory agents but also as hormones which have many physiological effects. This physiological action is largely responsible for the side-effects which tend to become manifest with prolonged administration of therapeutic doses far in excess of the patient's physiological needs.

A chapter on the pituitary-thyroid relationship by S. C. Werner has many clinical implications and brings out the value of thyrotropic hormone in the differentiating of primary and pituitary myxœdema.

A chapter on hormones and peptic ulcer by J. B. Kirsner summarizes current knowledge. This survey indicates no constant relationship between endocrine disorder and chronic peptic ulceration in man.

Other chapters include discussions of virilism, steroids and gonadotropins in gynæcology, disturbances of growth, mineral metabolism, and a clinical paper on differential diagnosis by L. J. Soffer.

The book will serve as a short postgraduate course in this rapidly changing field of medicine.

HUMAN HEREDITY

J. C. Neel and W. J. Schull, Heredity Clinic, University of Michigan. 361 pp. illust. $6.00. University of Chicago Press, 1954.

Associated with the current rapid development of human genetics in medical education, several new textbooks have appeared, the latest of which comes from the Heredity Clinic of the University of Michigan. Written by an outstanding human geneticist, Dr. Neel, in collaboration with a statistician, Dr. Schull, this most recent text discusses the techniques of analysis of problems in human inheritance.

The book is an important contribution for the more advanced student of human genetics. The treatment is comprehensive, with sections on physiological genetics (illustrated by albinism, alcaptonuria, sickle-cell anæmia, phenylketonuria, amaurotic idiocy, gout, and so on) and epidemiology, both being topics of particular interest to medical workers. Other sections deal with more standard topics such as modes of inheritance, linkage, genetic counselling, medicolegal aspects of genetic knowledge, and a discussion of eugenical applications. A chapter on twins points up the value of the twin method in medical research.

A satisfactory chapter is the one on mutations. The clear treatment of this most recent problem of the atomic age stems from the experiences of the two authors, both of whom have served in Japan on the Atomic Bomb Casualty Commission in Hiroshima.

The book emphasizes to a notable extent the methods of human genetics. This is indicated by the space allotted to a discussion of the statistical treatment of genetic data, to which several chapters are given over almost entirely; one deals with the estimation of genetic constants and another with analysis of family data. Unfortunately most students of the subject, lacking mathematical training, will find these sections difficult to follow, in spite of the care that obviously has been taken in their preparation. The applications of these methods to actual data are not as completely illustrated as they might be, particularly in the section on family material. An inexpensive supplement to this text, giving the mathematical solutions to the problems listed at the end of the chapters, would increase its teaching value and general usefulness.

The book is highly recommended for students with some knowledge of genetics and some facility in mathematics. Those without such backgrounds will find it less satisfactory. It should serve as a good reference book for medical research workers whose investigations may have genetical implications.

Canad. M. A. J.
Mar. 15, 1955, vol. 72

PROTOZOOLOGY

R. R. Kudo, Professor of Zoology, The University of Illinois, Urbana. 4th ed. 966 pp. illust. $11.75. Charles C Thomas, Springfield, Illinois; The Ryerson Press, Toronto, 1954.

The first edition of Kudo's *Protozoology* appeared in 1931 and immediately established itself as a "must" for the student and research worker in protozoology. Its outstanding feature has been the section on taxonomy and special biology, in which the author has included descriptions and illustrations of representative protozoa of all classes, together with keys to the families. The fourth edition retains the organization of the third but includes descriptions of many additional species. The portions dealing with medically important protozoa, however, have not been altered much in the revision.

In the section on general biology, considerable new material was noted in the chapter on variation and heredity. Revisions and additions of less extensive nature appear in the chapters on physiology and morphology. Greatly expanded lists of references at the ends of the chapters now include some early works as well as papers into 1952.

The book is of interest principally to students and research workers. However, medical libraries and laboratories will find it a useful reference work and introduction to the voluminous literature on the protozoa.

STUDIES IN SCHIZOPHRENIA

By the Tulane Department of Psychiatry and Neurology. Reported by Robert G. Heath, Chairman. 619 pp. illust. $9.35. Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders & Company, Ltd., Toronto 1, 1954.

The basic premise of these researches is that schizophrenia is associated with abnormalities of the "septal region," limited as follows by Heath: "The caudal border of this region is formed by the anterior commissure; the rostral extent is the tip of the anterior horn of the lateral ventricle. It extends medially to the midline space separating the hemispheres. The dorsal extent is the septum pellucidum proper and the base of the lateral ventricles. It extends ventrally to the base of the brain and laterally about 5 mm. from the midline . . . structures included . . . are the subcallosal gyrus, rostrum of the corpus callosum, olfactory tubercle, septal nuclei proper, subcallosal fasciculus, pyriform cortex, and various olfactory pathways. . . . In summary, then, the septal region is part of the olfactory system. From its anatomical relationships it would appear to be a correlating structure interposed between the higher neocortical level and the diencephalic and midbrain structures." (p. 3).

Evidence from animal and human studies, including neurosurgical, metabolic, electroencephalographic, intracranial electrostimulatory, psychological and clinical investigations, is presented in support of the basic premise. A section of the book is devoted to "Discussions" by invited participants from other centres.

The work presented in this book, while provocative of criticism, is solid research. Dr. Heath and his colleagues are to be congratulated for producing this excellent volume, which shows what a well-integrated, collaborative research effort can accomplish.

PREFRONTAL LEUCOTOMY AND RELATED OPERATIONS: ANATOMICAL ASPECTS OF SUCCESS AND FAILURE

A. Meyer, Professor of Neuropathology and E. Beck, Research Assistant, Institute of Psychiatry, Department of Neuropathology, Maudsley Hospital, University of London. 60 pp. illust. $2.00. Published for The William Ramsay Henderson Trust by Oliver and Boyd, London; Clarke, Irwin & Company Limited, Toronto 5, 1954.

This monograph is based on a lecture about the anatomical aspects of neurosurgery in mental disorders. It will interest the many teams of psychiatrists and neurosurgeons in this country who are attempting to evaluate, from their own experience, the rationale and value of all the variants of prefrontal leucotomy that are being advocated nowadays. The authors have correlated the clinical preoperative and postoperative story with observations of the brain at autopsy, in 102 cases that survived the operation by longer than five months. The amount of frontal lobe isolated appeared to be an important factor in securing benefit. Some regional significance was noted. There appeared to be greater improvement after isolation of mid-cerebral, orbital and cingulate sectors, and more severe changes of personality when there was isolation of dorsolateral and lateral white matter.

GROWTH AND DEVELOPMENT OF CHILDREN

E. H. Watson, Professor, and G. H. Lowrey, Assistant Professor, Department of Pædiatrics and Communicable Diseases, University of Michigan Medical School. 296 pp. illust. 2nd ed. $7.00. The Year Book Publishers, Inc., Chicago, 1954.

The transcending importance of the subject, knowledge of which represents the basic reason for the specialty of pædiatrics, made the first edition of this book an eagerly awaited event. It proved disappointing, not because of any inherent defect in the subject matter, but because it was essentially a handbook and treated this huge subject in superficial fashion. It has served a useful place, however, in pædiatric schools for convenient reference by undergraduates and junior postgraduate students.

The second edition is somewhat enlarged, particularly in the discussion of growth of the face and of the legs and feet. Only minor changes are found in the bulk of the subject matter. It will prove to be still more helpful than the first edition. We still await, however, a complete treatise on this most important subject.

BEING BORN

F. B. Strain. Revised and enlarged edition. 134 pp. illust. $3.25. Appleton-Century-Crofts, Inc., New York; S. J. Reginald Saunders & Company Limited, Toronto, 1954.

This is a new and revised edition of a book first published in 1936 by a well-known American educator. It is not a complete book on sex education, but a simple and attractive account of human reproduction for young children, literally a "child's guide to obstetrics." One wonders whether children in the age-group for which this book is evidently designed really need all the details given; but perhaps Mrs. Strain knows best and youngsters are interested in the details of embryology and heredity. If they are, this is the book for them; the information is conveyed correctly and painlessly.